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ANXIETY

Its Initiation, Communication and Interpersonal Management

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AND
A. RODNEY PRESTWOOD, M.D.
SAN FRANCISCO

. . . a little bit of nausea—helpless to retaliate—want to fight . . . to run . . . but . . .

THESE were the utterances of a patient as he broke out in sweat and clenched his fists. Simultaneously the therapist felt uneasy. Ninety per cent of all witnesses listening to the recording of this interview similarly felt uneasy.

The events underlying this and other related accounts were made the subject of a study bearing on the observation that anxiety is infectious, transmission proceeds at a rapid speed and a person's sensitivity to the anxiousness of other people is great. Experiments and observations were utilized in an attempt to reach a better understanding of the problems of communication, with special reference to the anxiety existing within the therapeutic situation.

SUMMARY OF THE CONCEPT OF ANXIETY

Reaction to danger is described in terms of anger, fear or anxiety.[1] The reaction to a danger cue, which Freud[1b] described as "real anxiety," is a warning mechanism which informs the person of an impend-

From the Division of Psychiatry, University of California Medical School, and the Langley Porter Clinic.

This investigation was supported by a research grant from the Division of Mental Hygiene, United States Public Health Service.

1. (*a*) Darwin, C.: Expression of Emotions, New York, D. Appleton & Company, 1910. (*b*) Freud, S.: The Problem of Anxiety, New York, W. W. Norton & Company, Inc., 1936; (*c*) The Justification for Detaching from Neurasthenia a Particular Syndrome: The Anxiety Neurosis, in Collected Papers, New York, International Psychoanalytical Press, 1924, vol. 1, pp. 76-106; (*d*) A General Introduction to Psychoanalysis, New York: Liveright Publishing Corporation, 1935; (*e*) Inhibitions, Symptoms and Anxiety, London, Hogarth Press, 1936; (*f*) New Introductory Lectures on Psychoanalysis, New York, W. W. Norton & Company, Inc., 1933. (*g*) Gantt, W. H.: Experimental Basis for Neurotic Behavior, New York, Paul B. Hoeber, Inc., 1944, p. 211. (*h*) Horney,

(*Footnote continued on next page*)

ing threat. The subsequent instigation of psychologic as well as physical preparedness for action is known as the alarm reaction,[2] which, in turn, leads to elimination of the interference or avoidance of the danger through fight or flight. The alarm reaction is a total organismic reaction designed for self preservation.

A so-called anxiety state develops when the person feels helpless and immobilized and when action becomes impossible either because of self inhibition or because of overwhelming environmental press.[3] Then the massive impact of stimuli on the organism, the feeling of danger and the expectation of defeat become so overwhelming that the person feels paralyzed. As a result, the preparedness for action cannot be consummated, and vascular, muscular, respiratory and endocrine phenomena[4] persist for undue lengths of time. This condition is felt by the individual as anxiety and tension.

Therefore, differentiation of anxiety states from fear and anger is characterized by the ability to act. In anger, impending danger or interference has been perceived as a threat which can be managed, fought and conquered; action is contemplated or already undertaken, and the behavior of the organism has been coordinated for this purpose.

K.: Our Inner Conflicts, New York, W. W. Norton & Company, Inc., 1945; (*i*) The Neurotic Personality of Our Time, New York, W. W. Norton & Company, Inc., 1937. (*j*) Kubie, L. S.: Instincts and Homeostasis, Psychosom. Med. **10**:15-30, 1948. (*k*) The Ontogeny of Anxiety, Psychoanalyt. Rev. **28**:78-85, 1941. (*l*) Ribble, M. A.: Anxiety in Infants and its Disorganizing Effects, in Lewis, N. D., and Pacella, B. L.: Modern Trends in Child Psychiatry, New York, International Universities Press, Inc., 1945. (*m*) Weisz, S.: Anxiety As a Symptom, Dis. Nerv. System **3**:394-399, 1942.

2. Wolff, H. G.; Hardy, J. D., and Goodell, H.: Studies on Pain: Measurement of the Effect of Ethyl Alcohol on the Pain Threshold and on the "Alarm" Reaction, J. Pharmacol. & Exper. Therap. **75**:38-49, 1942.

3. Ruesch, J.: The Infantile Personality: The Core Problem of Psychosomatic Medicine, Psychosom. Med. **3**:134-144, 1948.

4. (*a*) Cannon, W. B.: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton & Company, 1929; (*b*) The Wisdom of the Body, New York, W. W. Norton & Company, Inc., 1932. (*c*) Darwin.[1a] (*d*) Freud.[1e] (*e*) Kerr, W. J.; Dalton, J. W., and Gliebe, P. A.: Some Physical Phenomena Associated with the Anxiety States and Their Relation to Hyperventilation, Ann. Int. Med. **2**:961-991, 1937. (*f*) Kubie, L. S.: A Physiological Approach to the Concept of Anxiety, Psychosom. Med. **3**:263-276, 1941. (*g*) Landis, C., and Hunt, W. A.: The Startle Pattern, New York, Farrar & Rinehart, Inc., 1939. (*h*) Morgan, C. T.: Physiological Psychology, New York, McGraw-Hill Book Company, 1943. (*i*) Noble, R. C.: The Nature of the Beast, New York, Doubleday & Company, Inc., 1946. (*j*) Pepper, O. H. P.: Handicap of the Patient's Fears, J. Nerv. & Ment. Dis. **82**:639-651, 1935. (*k*) Richter, C. P.: Biology of Drives, Psychosom. Med. **3**:105-110, 1941. (*l*) Shock, N. W.: Physiological Factors in Behavior, in Hunt, J. McV.: Personality and the Behavior Disorders, New York, Ronald Press, 1944, vol. 1. (*m*) Weisz.[1m]

In fear, integrated action is initiated to avoid the interference.[5] If for internal psychologic or external environmental reasons fight or flight is impossible, fear and anger change into anxiety.

ELEMENTS INITIATING ANXIETY

A prerequisite to understanding mechanisms of communication used in the transmission of anxiety is study of its initiation. In reviewing the literature it became evident that information available could be grouped under the headings of excitation, cues and gestalt.

Intensity of Excitation.—Freud [1f, e] was the first to call attention to production of anxiety by mass stimulation, and more recently Landis and Hunt [4g] and Kubie [1k] have mentioned the similarity between the startle reflex and manifestations of anxiety, inasmuch as both are reactions of the body to massive and sudden stimuli. Experimental verification of this hypothesis is difficult, since extreme limits of tolerance cannot be tested without inflicting permanent damage on the human organism. Thus, reports of intense stimulations are limited to descriptions of war experiences,[6] of catastrophes [7] and of tortures (war crimes) consisting of intense stimuli of pain, heat, cold, light or noise in order to produce breakdown and eventually death of the individual.

Analysis of these reports would indicate that both the intensity of the stimulus and the suddenness of the increment are factors in producing disorganization of behavior.[8] Sensory stimulation within the habitually perceived range of intensity will not produce alarm reactions unless the stimulus represents a danger cue. Since no stimulus is apprehended as an isolated item but every one is apprehended in relation to others only, relative rather than absolute differences are

5. Mower, O. H.: A Stimulus Response Analysis of Anxiety and Its Role As a Reinforcing Agent, Psychol. Rev. **46**:553-565, 1939.

6. (*a*) Grinker, R. R., and Spiegel, J. P.: War Neuroses, Philadelphia, The Blakiston Company, 1945. (*b*) Grinker, R. R., and Spiegel, J. P.: Men Under Stress, Philadelphia, The Blakiston Company, 1945. (*c*) Kardiner, A., and Spiegel, H.: War Stress and Neurotic Illness, New York, Paul B. Hoeber, Inc., 1947. (*d*) Miller, E.: The Neuroses in War, New York, The Macmillan Company, 1940. (*e*) Bartemeier, L. H.; Kubie, L. S.; Menninger, K. A.; Romano, J., and Whitehorn, J. C.: Combat Exhaustion, J. Nerv. & Ment. Dis. **104**:358-525, 1946. (*f*) Kubie.[1j] (*g*) Menninger, W.: Modern Concepts of the War Neuroses, in the Yearbook of Psychoanalysis, Chicago, The Year Book Publishers, Inc., 1947, vol. 3, pp. 227-242. (*h*) Romano, J.: Anxiety, in Teaching Therapeutic Medicine, New York, The Commonwealth Fund, 1947. (*i*) Whitehorn, J. C.: Changing Concepts of Psychoneurosis in Relation to Military Psychiatry, A. Research Nerv. & Ment. Dis., Proc. **25**:1-10, 1946.

7. Goldstein, K.: On So-Called War Neuroses, Psychosom. Med. **5**:376-383, 1943.

8. Pavlov, I. P.: Neurosis in Men and Animals, Correspondence, J. A. M. A. **99**:1012-1013 (Sept. 17) 1932.

perceived. Perception of differences and their relative lag is a function of the cortical activity,[9] inasmuch as the sensation may be proportionate to the logarithm of the stimulus.[10] While the stimulus leaps ahead by ratios, the sensation plods along step by step, a phenomenon which protects the organism from intense stimulation. Whenever goal-directed behavior for reduction of tension cannot be initiated, the organism nonetheless possesses a few other safety valves. Thus laughter, vicarious gratification of other needs, withdrawal or anticipation of tension reduction through fantasy processes may be mentioned. But regardless of these, under continued intense stimulation a limit of excitation will eventually be reached which cannot be mastered by the organism. This point may be reached late when an individual functions at an optimum, or early if fatigue, malnutrition or disease have weakened the organism, as observed in flying personnel,[11] prisoners of war and hospital patients. Then intense anxiety will develop in the individual, behavior will become disorganized, physical and psychologic shock reactions can develop and death may follow.

Cues.—The second cluster of factors contributing to the development of anxiety concerns specific warning signals or cues, which in the past were associated with danger situations. A cue is defined as a signal used to simplify solution of complicated problems, enabling the organism to focus on a few relevant signals instead of watching a good many thousands of irrelevant ones.[12] If such a cue is perceived either exteroceptively (taken from the environment) or proprioceptively (taken from the organism itself), anxious expectation and anticipation of recurrence of an old unpleasant or threatening situation will produce an alarm reaction; perception of cues related to nonthreatening and familiar events will have a relaxing effect on the organism.

Gestalt.—Reaction to stimulation is determined not only by intensity and suddenness of the stimulus, with its cue values, but also by its relation to other sets of stimuli [13] and their arrangement in time and space. This togetherness and totality of impressions may be called its gestalt.[14]

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9. Wundt, W.: Grundzüge der physiologischen Psychologie, ed. 5, Leipzig, J. Engelmann, 1911, vol. 3.

10. Fechner, C. T.: Elemente der Psychophysik, Leipzig, Breitkopf & Härtel, 1860.

11. Armstrong, H. G.: Principles and Practice of Aviation Medicine, Baltimore, Williams & Wilkins Company, 1939.

12. (*a*) Ruesch, J.: Experiments in Psychotherapy: I. Theoretical Considerations, J. Psychol. **25**:137-169, 1948; (*b*) Individual Social Techniques, J. Soc. Psychol. **29**:3-28, 1949.

13. Lewin, K.: Principles of Topological Psychology, New York, McGraw-Hill Book Company, 1936.

14. Kohler, W.: Gestalt Psychology, New York, Liveright Publishing Corporation, 1947.

Whenever impressions from the environment form a pattern and are perceived as being of approximately equal intensity, and when they appear to be coordinated, harmonious, regular, rhythmic and familiar, the person feels more at ease than when there is roughness, irregularity and strangeness. This observation seems to apply already to the human fetus in utero,[15] for the rate of the fetal heartbeat can be increased if a vibrating tuning fork is placed on the mother's abdomen, if a doorbell buzzer is placed over the fetal heart or if loud noises occur in a nearby room.[16] It also applies to the great apes, which can be terrified by large and unfamiliar objects or by strange events.[17] Thus, a group of gibbons was paralyzed with terror when trees were being felled, and many were crushed under the falling trees. Unfamiliarity with mutilated or unresponsive bodies creates alarm in both man and chimpanzee. Alarm with regard to strangeness is therefore not determined by the particular source of sensory excitation but by discrepancy of the total pattern from that which previously had been frequently experienced by the subject. The same principle can be applied to interpersonal relations. Unconsciously most persons combine the impressions gained about another person with their own subjective reactions into a total gestalt. If there is a resulting unity of fit and feeling of well-being, the basis is established on which a good interpersonal relationship can develop. If there is strangeness and disunity of fit, an alarm reaction is likely to occur, interfering with communication.

MECHANISM OF COMMUNICATION

In applying the information discussed in the preceding section to study of communication mechanisms, one recognizes immediately that factors of intensity, cue values and gestalt criteria also operate in transmission of alarm signals. In this section, then, an attempt is made to specify more precisely the nature of these factors as they apply in daily life and in the therapeutic situation in particular.

Transmission of Alarm Signals in Daily Life.—Throughout the animal world there are many specific features related to color, shape, sound, odor and motion which are instrumental in transmitting signals. In the presence of excitation, the lion spreads his mane and waves his tail with its conspicuous dark patch, the bear exposes the striking spots

15. Greenacre, P.: The Predisposition to Anxiety, Psychoanalyt. Quart. **10**:66-94, 1941.

16. Sontag, L. W., and Wallace, R. F.: Changes in Rate of Human Fetal Heart in Response to Vibratory Stimuli, Am. J. Dis. Child. **51**:583-589, (March) 1936.

17. (*a*) Kohler, W.: The Mentality of Apes, New York, Harcourt, Brace and Company, Inc., 1925. (*b*) Yerkes, R. M., and Yerkes, A. W.: The Great Apes, New Haven, Yale University Press, 1929.

on its breast, the deer flashes its tail [41] and the fiddler crab brandishes a bright red claw; the comb of the rooster, the wattles of the turkey, the blue face of the mandrill, the red buttocks of the baboon, all become brighter during excitation and are conspicuously displayed.[41] Certain birds use the markings of their wings to convey to others the presence of danger,[18] while the alarm note of chicks, the harsh "krek" of the moor hen,[19] the scream of the chimpanzee [17a] and the cry of the wild pig [20] are vocal means for alerting other members of the animal group. The colonies of murres along the North Atlantic coast depend to a large extent on the warning cries of the more alert and vocal gulls for their self presevation.[41] Gestures, such as the stretching of the neck of a gull or the lifting of the wing of a duck, induce other members of a flock to fly away. The ape seems to be more dependent on vision than on hearing, for this animal reads the minds of its fellows and interprets attitudes, acting much like a human deaf-mute.[17b] Gesture, posture, position, movements of the mouth, head and body, facial expression and changes, especially of lips, jaws, cheeks, ears, eyes and brows, conditions and changes of tension in the body, of color and moistness of the skin, position of the hair, vocal sound production and secretory as well as excretory changes are used by apes for communication.[21]

In human beings transmission of danger signals occurs through various channels. Throbbing pulsations, blanching, blushing, sweating, tension, strained posture, certain forced motions, twitching, tremor, general restlessness, fatigue, sighing and rapid shallow breathing are all signs of an alarm reaction which can be observed visually and in the therapeutic situation. Speech and associated manifestations such as high-pitched, shrill, loud or tremulous voice, arrhythmic alternation between a high and a low pitch, sudden spurts, outbursts or rushes of words, overtalkativeness, lack of periods, pauses and silences, unfinished words and sentences, interruption of other speakers, snapping of words, sudden variations in speed, repetition of words, insistence, forced or inappropriate laughter are auditory signs which communicate uneasiness. The reverse picture can be observed in people whose uneasiness is communicated through long pauses, meager production of words, hesitating and faltering voice or introduction into speech of inarticulate sounds such as "ah" and "oh" or words such as "and," "or" or "well," which

18. Lorenz, K.: Der Kumpan in der Umwelt des Vogels, J. f. Ornithologie **83**:137-213 and 289-413, 1935.

19. Morgan, C. L.: Animal Behavior, London, Edward Arnold & Company, 1915.

20. Medlicott, H. B.: The Evolution of Mind in Man, cited by Morgan, C. L.: Introduction to Comparative Psychology, London, Scott Publishing Company, 1904.

21. Kohler.[17a] Yerkes, R. M.: Almost Human, New York, The Century Company, 1925.

are then used as conjunctives for tying together unrelated sentences. Such signs of uneasiness were observed in sound recordings of therapeutic sessions, which neutral witnesses declared as communicating to them a certain degree of anxiety.

Nonverbal communication is used by actors, who frequently take a short play, play it first as a tragedy and then, using the same words, play it as a comedy. Here the audience seems to react to timing rather than to the words used.[22] Similarly, actions and movements become even more relevant when one is traveling in a foreign country. Frequently the traveler has to make judgments solely on the basis of the native's actions, which surprisingly can become a more accurate means of communication than the interpretation and translation of words.[22]

Experimental Transmission of Anxiety Through Sound Cues.—In applying to the study of communication within the therapeutic situation information about anxiety derived from observations of daily life, the question arose as to how anxiety is transmitted under interview conditions. Furthermore, the question was raised whether anxiety is forcibly transmitted as in the animal world or whether an individual can retain freedom of action in the presence of anxiety of others. From clinical observations it seemed that young psychiatrists reacted to the patient's feelings of anxiety and alarm much more readily than to feelings of depression or guilt. This seemed to indicate that in certain circumstances human beings are forced to react to the anxiety of others. In order to answer the question whether personal participation and physical presence are necessary or whether mere listening to the recording of an anxious interview would transmit uneasiness and infect the listener, the following experiment was designed.

Experiment 1: Out of a selection of more than two hundred hours of sound recordings of therapeutic interviews (wire recorder) the experimenters isolated passages which seemed to them to express varying degrees of anxiety and anger either on the part of the therapist or on the part of the patient. These passages were limited to five minutes and transcribed in random order onto other spools. Then these spools were played back to an audience of 22 psychiatrists who were instructed to choose one of three types of subjective reactions as described in the table. After listening, the 22 young psychiatrists were rather anxious or angry themselves: Some started to criticize one another; some began to argue; some became fidgety and nervous, expressed the desire to leave the room or moved restlessly on their chairs.

Statistical analysis of the data revealed a clear distinction between the responses of the audience to recordings of anxious interviews on the one hand and angry or relaxed interviews on the other ($P < 0.01$).

22. Chapple, E. D.: Measuring Human Relations: An Introduction to the Study of the Interaction of Individuals, Genet. Psychol. Monogr. **22**:3-147, 1940.

Reaction to angry interviews as compared with reaction to relaxed interviews showed a similar but less marked difference ($P < 0.03$). It was possible to demonstrate statistically that the audience reacted primarily to anxiety and anger and not to other personality features, since the reactions of the audience to repeated recordings of the same therapist with a number of his patients were significantly different ($P < 0.01$), and responses of the audience to each of the two doctors

Subjective Responses of Psychiatrists to Recordings of Interviews
(N = 22)

Interview sample	Do you feel relaxed? at ease? comfortable? interested? friendly? warm? understanding?	Do you feel not quite at ease? uncomfortable? bored? sleepy? scornful? restless? distant? apprehensive?	Do you feel tense? disturbed? angry? resentful? disgusted? depressed? embarrassed? irritable? fearful?
		A.—Relaxed Interviews	
Dr. A—patient 2	11	11	0
Dr. A—patient 3	13	8	1
Dr. B—patient 6	9	12	1
Dr. B—patient 4	10	11	1
Dr. B—patient 9	11	11	0
Total	54	53	3
		B.—Anxious Interviews	
Dr. A—patient 10	2	13	7
Dr. A—patient 1	4	7	11
Dr. A—patient 2	4	17	1
Dr. B—patient 4	7	12	3
Dr. B—paitent 5	4	10	8
Total	21	59	30
		C.—Angry Interviews	
Dr. B—patient 6	7	15	0
Dr. B—patient 7	8	12	2
Dr. B—patient 8	8	12	2
Dr. A—patient 1	5	15	2
Dr. A—patient 2	8	12	2
Total	36	66	8

were not significantly different ($P < 0.20$). This indicates that the audience did not react primarily to structural personality features of the doctor. To a less extent ($P < 0.10$) the same trend holds for reactions to the patients when recorded at different times interacting with their respective therapists. This indicates that reactions of this audience were influenced more by patient than by psychiatrist, but, on the whole, responses were to interaction features rather than to structural personality variables. From this experiment it can be concluded that anxiety and anger as expressed in interviews and recorded can be transmitted to an audience and force their participation. Apparently sound recordings contain elements which transmit anxiety and anger.

Experiment 2: Further attempts were carried out to isolate the elements which transmit anxiety. The following measurements were made of five minute samples of recorded interaction: (1) the average number of words said by therapist or by patient in one minute of interview; (2) the average rate of words spoken per minute—that is, the speed of speech of one individual whenever he talked; (3) the time duration of pauses during which either patient or therapist interrupted himself for reflection and then resumed the stream of talk; (4) the time duration of silences (neither person speaks) after which a shift of action occurred from patient to therapist, or vice versa; (5) the number of times one person interrupted another.

In applying these indexes to the study of one and the same therapist in his behavior with several patients, the number of words spoken by the therapist varied from 4 to 111 per minute of interview, depending on the situation, whereas his speed of speech showed more consistent trends. The habitual speed for most people varies between 200 and 300 words as calculated per one minute, the extremes ranging from 147 to 342 words per minute. In therapist A, a consistent and statistically significant increase in speed of speech was observed whenever he was confronted with an angry patient, simultaneously increasing the length of pauses in his speech. When these subtle changes in the rate of speech were then related to the number of words spoken, it was found that therapist A spoke more words when the patient was relaxed but simultaneously decreased his rate of speaking, while therapist B spoke more and increased his rate whenever the patient became angry. On application of these indexes to the study of patients, it became clear that the patients' speech was either faster or slower and the number of words said either greater or smaller when anxious or angry than when relaxed.

When these smaller samples were compared with the total interview from which they had been taken, it became clear that deviations and changes either in pitch and intensity of the voice, number of words spoken, speed of speech and duration of pauses and silences were likely to announce to the listener a change in reaction of the other person. This reaction did not seem to be uniform from patient to patient or from therapist to therapist but seemed to be specific for any single individual. These findings would explain the commonly observed phenomenon that on closer acquaintance people react more quickly and understand one another better because they have learned to perceive these subtle changes and have understood the individual rhythms of the other person.

Experimental Transmission of Anxiety Through Written Verbal Cues.—After having established the infectious nature of anxiety through personal contact and through listening to sound recordings, the question was raised whether the printed word—that is, the content of a conversa-

tion—would reveal the presence of anxiety to a neutral observer. Furthermore, inquiry was needed to establish whether the printed word could force participation on the part of the reader, or whether the latter would merely perceive—that is, observe—anxiety without being infected personally. For this purpose the following experiments were designed.

Experiment 3: Interviews previously recorded were typed out and presented to a group of four expert witnesses consisting of psychologists and psychiatrists. These were asked to read the interviews, to record subjective impressions, to make comments and to rate certain personality variables on a specially prepared rating sheet. In a second step, the witnesses were then asked to listen to the original sound recordings and again to make comments and to rate the interviews. In a third step, then, the witnesses were allowed to interview the therapist to obtain his subjective feelings to complete the picture. The purpose of this experiment was to identify the nonverbal anxiety variables which were revealed as gradually more and more participant-derived information was added to the original verbal content.

The results of this experiment, which was repeated with 6 different patients seen by 3 different therapists, warranted the following conclusions. In reading the interviews, observers frequently were unable to ascertain clearly the meaning of the patient's verbal productions without long and detailed study. This relative lack of understanding made it difficult to discover cues related to anxiety, though experienced therapists could generalize as to the presence of anxiety from knowledge of other cases but without being able to put their fingers on the crucial clues. The addition of sound recording supplied information which enabled the observer to get an immediate impression of nonverbal, social and manipulative approaches used in the interview. Timing, intensity and emphasis, as well as modulations of the voice, enabled clear detection of phenomena such as nagging, whining, hostility, coyness, playfulness, seductiveness, amusement, tearfulness, evasiveness and aloofness. All became more apparent on listening. Above all, the ability of the patient and of the therapist to express himself sincerely could be judged only on listening. In reading the interview, observers were unable to detect whether the spoken material was really an expression of concern of the patient or whether it was used as defense mechanism to hide and control anxiety. Addition of the third step—namely the personal comments of the respective therapists—added the final touch to understanding of the material. The gestalt of the total situation could be understood only through the therapist's participant-gained information. In conclusion, it may be said that in reading the anxiety perceived is not particularly infectious and does not force participation. Overt anxiety

and anger, as well as successful communication, can be isolated after hearing the recorded interview. Well controlled anxiety and partial communication are likely to be detected only after the therapist personally has been interviewed.

Experiment 4: In this experiment an attempt was made to analyze the verbal symbols contained in anxiety and anger recordings. A comparison of 300 word samples of speech of 8 patients in three emotional states—labeled relaxed, anxious, and angry—revealed significant differences (the chart) which were arrived at by applying a simple analysis of words and expressions. The following aspects were analyzed and counted:

(1) Frequency of expressions of feelings: e. g., "I felt bad."

(2) Frequency of abstract nouns used to express abstraction: e. g., "thought," "life," "love."

(3) Frequency of concrete nouns: "house," "tree," "bird," "ship."

(4) Frequency of personal references: (*a*) nouns referring to persons, e. g., father, mother, sister or teacher or animals used in the sense of a person; (*b*) personal pronouns, such as "I," "he," "she," "we."

(5) Frequency of (*a*) self-instigated action in which the speaker is instigator—e. g., "I ran away"; (*b*) of other-instigated actions involving the speaker passively, in which some one or something else was the instigator—e. g., "I was taken to school," "I was forced to—."

(6) Frequency of qualifications: (*a*) subjective qualifications, such as "happy," "strong," "successful," "sad," "poor," "weak"; (*b*) objective qualifications, such as "American," "four," "green."

The results of this analysis are graphically demonstrated in the chart and may be interpreted as follows: increase in number of words referring to feelings, personal pronouns and subjective qualifications seem to be perceived by the listener as a state of excitement and of self concern in the speaker. In contrast, reduction in number of subjective qualifications and of personal pronouns with simultaneous increase in use of concrete nouns and objective qualifications seems to be perceived as representative of a more relaxed attitude, denoting an objective rather than subjective state of emotions of the speaker. Anger samples differed from anxiety samples inasmuch as in anger expressions of self-instigated action increased in frequency consistently. These findings bear out the initially summarized concept that in anxiety the patient's main concern is with self and feelings, while in anger the main emphasis lies in action.

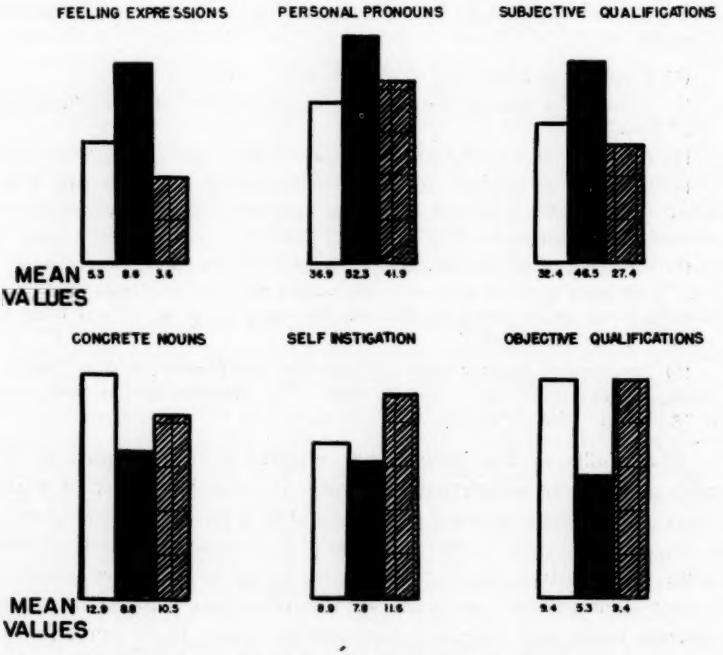
These four experiments thus established the following facts:

Anxiety can be transmitted through sound alone. The cues operating within the therapeutic situation are primarily acoustic. They manifest themselves in frequency, amplitude and timing characteristics.

Additional anxiety cues are found in the semantic character of verbal symbols. However, the acoustic cues seem to be more universal, to be more easily apprehended and to elicit a quicker response than the semantic cues, perception of which requires a longer exposure.

Listening to recordings of anxious people forces a reaction and makes an unbiased observation difficult.

Transcription of a conversation of anxious people may suggest to the reader the presence of anxiety. However, reading does not force par-



Analysis of verbal symbols (words and phrases) in recordings of 300 word samples from 8 subjects in three emotional states (relaxation, anxiety and anger). White columns indicate relaxation; black, anxiety; cross hatched, anger. The significance of the mean values can be appreciated in considering the number of patients in whom increases or decreases occurred during anxiety or anger. Increases occurred during anxiety in expressions of feeling (7 out of 8 patients); personal pronouns (8 out of 8 patients); subjective qualifications (8 out of 8 patients). Decreases occurred during anxiety in concrete nouns (6 out of 8 patients); objective qualifications (7 out of 8 patients). Increases occurred during anger in: references to self-instigated action (8 out of 8 patients).

ticipation, and only the subsequent addition of sound gives the listener an opportunity to understand fully the interaction situation.

INTERPERSONAL MANAGEMENT OF ANXIETY

Alleviation of Anxiety Through Personal Contact.—Since anxiety and social contact are intimately related phenomena,[23] the next question pertained to methods of alleviation. Before considering the therapeutic situation, review of other relationships may contribute to a better understanding.

Anxiety in infants derives principally from three types of dangers: there are the biologic threats, such as hunger or thirst; there is loss of the mother, with its implied loss of support, or prolonged separation from her, and there is frustration of spontaneous activity. Any one of these dangers can lead to development of alarm reactions, which, in turn, are either attenuated or magnified by behavior of persons surrounding the child. Principal channels for transmission or alleviation of anxiety in the infant are touch, rhythmic movements and sound. Thus, touch of the mother has a definite biologic implication in the regulation of breathing and nutritive functions of the child. Certain body positions contribute to development of psychologic ties between mother and child, supporting the suggestion that the nervous system needs some sort of stimulus—feeding or rhythmic vibratory movement, such as rocking—to facilitate its development. Children who do not get this form of mothering in the early months frequently substitute for it themselves with body rolling.[11] The third channel of contact is sound. Newborn babies show a violent startle reaction to loud and sudden noises, and after the first weeks of life it is evident that the human voice begins to exert a peculiar soothing effect on the child. Speaking softly or singing contributes toward establishing a better relationship between mother and child. Whenever the mother does not handle these channels of communication appropriately, she either generates tension in the child or transmits her own anxiety.[24] This fact was clearly illustrated during the war by children who went through bombing or were hurt or buried under debris for days without food. They were relatively free

23. (*a*) Saul, L. J.: Emotional Maturity, Philadelphia, J. B. Lippincott Company, 1947. (*b*) Sullivan, H. S.: The Meaning of Anxiety in Psychiatry and in Life, Psychiatry **11**:1-13, 1948.

24. (*a*) Bettelheim, B., and Sylvester, E.: Physical Symptoms in Emotionally Disturbed Children, Psychoanalytical Study of the Child, series no. 3, New York, International Universities Press, Inc., 1948. (*b*) Despert, J. L.: Children's Reactions to the War, New York, The Josiah Macy Foundation, 1942. (*c*) Freud, A., and Burlingham, D. T.: War and Children, New York, Medical War Books, 1943. (*d*) Freud, S.: The Justification for Detaching from Neurasthenia a Particular Syndrome: The Anxiety Neurosis, in Collected Papers, New York, International Psychoanalytical Press, 1924, vol. 1, pp. 76-106. (*e*) Levy, D. M.: Release Therapy, Am. J. Orthopsychiat. **9**:713-736, 1939. (*f*) Szurek, S.: Collaborative Psychiatric Therapy of Parent-Child Problems, Am. J. Orthopsychiat. **3**:511-516, 1942.

from anxiety if the mother was able to withstand this experience without being disrupted emotionally, while conversely anxiety and tension on the part of the mother were readily transmitted to the child like an infectious disease.[6h] In the presence of anxious mothers, children have to learn to handle their excitation alone, resulting in a generalized retraction of functions of awareness and sensitivity ("shock" children), in discharge of tension through anxiety-alleviating activities such as thumb sucking, retention of stools, breath holding or other automatic movements.[25]

It has been definitely established that closeness to nonanxious persons reduces anxiety, whereby contact seems to be more anxiety-alleviating if the person is a beloved one, as contrasted with a stranger.[26] This phenomenon can be observed in both human beings and animals. Just as there is a natural impulse for the normal mother to alleviate the anxiety of the child by picking it up, the mother animal will hurry along to protect the young. Similar behavior can be observed in the farmyard, when a hen's cackling in fear will bring a diligent cock hurrying along to her aid, obviously excited and furious.[17a] In the laboratory, neurotic cats overcome their feeding inhibitions when placed in experimental situations with another cat which possesses normal responses to the same anxiety-producing signal.[27] Manifestations of a neurotic dog in a laboratory were alleviated by the presence of a person standing by him during experiments.[28] Sheep which had been made neurotic were observed to show little restless activity whenever the experimenter was nearby.[26a] Dogs are commonly known to sense the mood of their masters. Anxiousness of a trainer makes the dog confused, but if the trainer is at ease the dog learns rapidly. The same is known to be true in apes, which, having ability to detect courage, timidity, frankness or deception, like or dislike and anxiety in human beings, will react accordingly.[21b]

Reich,[29] in searching for an understanding of these peculiar phenomena, stated that anxiety in human beings is expressed in a constriction of the peripheral blood vessels accompanied with a psychologic as well as a physiologic retraction of the individual toward the center, in analogy to the retraction of pseudopodia and antennas in lower animals. Contact

25. Bettelheim.[24a] Ribble, M. A.: The Significance of Infantile Sucking for the Psychic Development of the Individual, J. Nerv. & Ment. Dis. **90**:455-463, 1939.

26. Anderson, O. D., and Parmenter, R.: A Long-Term Study of the Experimental Neurosis in the Sheep and the Dog, Psychosom. Med. 2: (no.) 3 and 4, 1941. Despert.[24b] Ribble.[11]

27. Masserman, J. H.: Behavior and Neurosis, Chicago, The University of Chicago Press, 1943.

28. Liddell, H. S.: The Experimental Neurosis, Ann. Rev. Physiol. **9**:569-580, 1947.

29. Reich, W.: Character Analysis, for Psychoanalysts in Practice and in Training, ed. 2, Orgone Institute Press, 1945.

apparently produces dilatation of these peripheral blood vessels, and the heat stimulus is supposed, through dilation of blood vessels, to alleviate anxiety.

Patterns of Interpersonal Relations.—The fact that a nonanxious adult can alleviate anxiety of an anxious infant seems to constitute the basis for all future interpersonal relations. Depending on these early experiences, a person when anxious will either seek the company of others to share anxiety or will use defense mechanisms for handling this anxiety alone. In the former case, the person will attempt to adapt to others and to the prevailing social order in order to be able to share anxiety, while in the latter case an attempt will be made to control others. In adaptation, the endeavor is oriented toward establishment of an anxiety-alleviating interpersonal relationship. In control, the goal is to bring about a situation in which the existing defense mechanisms can be utilized best. Among these defenses are activities designed to alleviate anxiety through substitute gratification, such as overeating, drinking, smoking or sexual promiscuity.[30] Other defenses are designed to control the self expression of emotions so that anxiety will not be revealed to others, and there are further defenses designed to prevent anxiety-producing situations from arising in the first place.

In social interaction these defenses, however, are not quite foolproof and a certain amount of leakage of anxiety usually will occur which affects other persons in particular ways. There are people, for example, who appear to be calm, efficient, orderly, punctual and attentive. However, at times of emergencies, when fire, earthquake or bombing may challenge the vital needs of an individual, some among these controlled people tend to become highly anxious and eventually to break down. Apparently their mechanisms are insufficient to manage anxiety, which in view of vital threats, grows to such proportions that it leads to total disorganization of behavior. In turn, slightly anxious persons who in daily life are less efficient and slightly emotional, who might miss their streetcars or forget their umbrellas, are uneasy about going out in rough weather and are occasionally intemperate in their expressions tend to tolerate their anxiety in emergency situations much better. These people seem to possess the ability to discharge anxiety little by little and in interpersonal relationships. Thus, in a social situation the calmness and compulsive manner of a person may be sensed by others as a desperate need to keep anxiety under control; as a matter of fact, it then conveys to the other person the idea that the situation is so dangerous that extreme efforts are needed for its management. Such an impression will generate anxiety, anger or apprehension in the second person.

30. Mowrer, O. H.: Anxiety-Reduction and Learning, J. Exper. Psychol. 27:497-516, 1940. Romano.[6h] Ruesch.[12b]

People who in social situations tend to alleviate their anxiety through a process of sharing use the mechanisms of expression and communication, while those people who tend to control their anxiety use the mechanisms of communization [31] and manipulation. Communication is bound to the use of signs, which in the case of human beings are predominantly verbal and to a lesser degree gestural. True communication depends on understanding of the general meaning of signs (semantics), on understanding of the interrelationship of the signs among themselves (syntactics), and the interrelationship of the individual and the sign (pragmatics).[31] True communication can be achieved only when there is mutual understanding of semantics, syntactics and pragmatics. In the process of communication, then, perception of the external sign is followed by subjective identification through feelings [23a] such as anger, anxiety, fear, shame, guilt and depression or satisfaction. In true communication between two persons the external sign is used by one to elicit in the other these specific feelings and associations which when combined with the external sign will transmit the correct meaning to that person. This, of course, can be achieved only through long personal contact between the two and through the background of a common culture.[12a]

The principal distinction between communication and communization is to be found in the motivation of persons engaging in social contact. In communization the intent of the person is not to communicate, but instead, a common denominator is selected in order to establish a certain degree of commonness and to avoid the anxiety of strangeness. Activities, interests, possessions, health or the weather may be utilized as topics in common for the establishment of contact. Frequently nothing need be said at all, if, for example, events occur which all participants witness, since each participant then knows that every other individual through the common experience will have a limited understanding. Communization is a phenomenon observed in a variety of organizations and social groups, such as golf clubs, yacht clubs and country clubs. It also inevitably occurs in times of catastrophes and emergencies. There, a common danger cue, such as an earthquake or an epidemic, instil fear, fright and panic, and this common experience binds all participating persons together. Communization then partially substitutes for communication.

Similar to the process of communization is the tendency to manipulate others by means of words, not with the intent to express something but with a desire to change the external situation. Usually conflict in terms of words, social action or physical violence is the result unless the

31. Morris, C. W.: Signs, Language and Behavior, New York, Prentiss-Hall, Inc., 1946.

other person demonstrates a willingness to be manipulated, because of need for dependence,[8] for example, or social masochism.[32] Attempted manipulation may not be obvious on initial contact with a strange person. At first, words uttered by the other person may be taken as an indication of sincere expression, but soon discovery may follow that expression on the part of the other person does not occur in unison with thought and feelings. In such an instance, words are really manipulated like materials or objects and there is no fusion or feelings, thought and action. It soon becomes obvious that either the feelings, actions or thoughts of such a person are not appropriate. The result is that such persons cannot share anxiety with others because they cannot express themselves completely. Instead, they seek to manipulate others, and this contact then partially eases their own anxiety. People of this kind tend to form teams with others, being bound together by laws of cause and effect, complementation or imitation. One person initiates something which is complemented or completed by responses of the other, or one person imitates or forces the other to imitate. These forms of social contact then substitute for communication.

Annihilation, identification, causation and complementation are all examples of these manipulative contact methods which substitute for true expression. They constitute infantile methods of social interrelation which can be clearly understood if one considers that manipulative ability for other persons develops earlier phylogenetically and ontogenetically than the verbal methods of expression and the language functions as a whole. In the process of true maturation, then, manipulation and language functions are fused. Prerequisite to this process of fusion is the development of signs. As the child learns to connect his inner feelings with the external cues, he goes through successive stages in which the majority of signs derive first from the body sphere, derive then from the action sphere and later pertain to verbal symbolization.[33] Thus the mature person learns to get physical release from expression in verbal or gestural terms, while the immature personality has to concretize in terms of carrying out detailed physical actions or establishing contact with the original objects themselves before release is found. Imperfect fusion of language functions with action is expressed in a variety of psychopathologic states involving magic-thinking, psychopathic acting out or organ expressions. In contrast, the maturer person openly admits the existence of anxiety; he attempts to share it with others, and he is not particularly interested in manipulating others unless it is with their approval. Hence it becomes obvious that the

32. Berliner, B.: The Concept of Masochism, Psychoanalyt. Rev. **29**:1-15, 1942. Berliner, B.: On some Psychodynamics of Masochism, Psychoanalyt. Quart. **16**:459-471, 1947.

33. Smith, M.: Communicative Behavior, Psychol. Rev. **53**:294-301, 1946.

degree of fusion between language and manipulative functions determines to a large extent the intricate patterns of interpersonal relations.

Experimental Alleviation of Anxiety of Patient Through Self Expression of Therapist.—Experiment 5: In order to investigate whether expression and communication on the part of the patient could be influenced through expressive behavior of the therapist, 5 subjects were studied in their longitudinal development of interpersonal relations with the therapist. After each session, which was recorded, a group of witnesses consisting of psychiatrists and psychologists listened to the interviews again. Sincerity, control and free expression of anxiety were subjects of study, and predictions were made of the expected behavior in the next and subsequent sessions.

The results of this experiment revealed that the predictions of the patient's future behavior were based only in part on the patient, the other part being determined by the therapist's management of his own anxiety. If in the process of mutual adaptation in the therapeutic situation the therapist expressed himself in unison, if he did not attempt to control, if he promoted communication and if he did not manipulate beyond the necessary minimum, the patient sooner or later followed suit. If the therapist was sincere, frank and direct and if he could express his own anxiety to the patient in communicable terms, the patient was not disturbed by it. If, however, the therapist attempted to control his anxiety, the patient gradually became more and more anxious. Thus, one can say that if anxiety were overtly expressed in communicable terms either on the part of the therapist or on the part of the patient, the interpersonal relationship improved and anxiety was less infectious. The expression of anxiety on the part of the patient was promoted through freedom of expression on the part of the therapist, while control on the part of the therapist fostered control mechanisms on the part of the patient. Through these tools the therapist was able to gage the rate at which anxiety could safely be communicated, preventing a flood which might have overwhelmed the patient and led to breakdown before a sound relationship could be established.

Experiment 6: Since it is obvious that previous training and tradition prevent free expression of anxiety in our society,[6d] it was thought that even when the therapist did express himself freely in an interview a certain amount of anxiety was likely to be controlled. The residual control was thought to be associated with the degree of participation of the therapist in the therapeutic situation. Participation would be defined as a situation in which a person assumes a role requiring interaction, whereas observation implies a role which does not require a person to interact. The peculiar position of the psychotherapist

requires alternation of roles of observer and participant: As a participant, he is exposed to the direct transmission of anxiety and anger; as an observer, he is able to observe the effects of experiences gained as participant. In order to demonstrate the interrelatedness of these two features, the following experiment was designed.

An original interview between a patient and a therapist was recorded. The subsequent day the interviewer then was asked to relisten to his session and to make comments on the interview as well as on his own state of mind. This performance was repeated several times at varying intervals until the therapist reached a somewhat consistent opinion about himself and his roles, functions and actions in the interview. This usually was achieved after four or five relistening sessions, occurring approximately during one week's time without renewed contact with the patient. The results of this experiment indicated that uniformly every therapist became anxious on hearing for the first time his performance in an interview. This anxiety then gradually disappeared on relistening four or five times until a certain level of stability was reached. After a varying number of experiments the surprise of the therapist lessened, but with each new patient even experienced therapists were astonished to discover features of which they were unaware.

In explaining this peculiar phenomenon, one has to consider that every person possesses stereotypes regarding his own behavior in group situations. This concept exerts a controlling function on the spontaneous behavior of a person and at the same time makes self observation difficult. As he listens to his recorded interview, anxiety develops because for the first time the therapist's participant-gained impression is fully translated into observer-gained information without the controlling influence of his own ideals. In the course of this process distortions of reality as well as discrepancies perceived from comparing actual behavior with the ideal concept create anxiety. Furthermore, in a social situation a great many control mechanisms are used to hide anxiety, which obviously become superfluous when one has a session by oneself, listening alone in a room to a recording. Easing up on the control mechanisms releases the original anxiety, enabling the listener to relive the interview under more favorable conditions with more awareness and less control.

The therapist's self ratings and the comments regarding the patient changed from session to session, revealing approximately the following trends. In the original interview emotional reactions such as anxiety, anger, fear, guilt, shame and depression were observed by the therapist to exist in the patient and usually tended to be overrated. On relistening for the first time, some of these features originally attributed to the patient were recognized as factors pertaining to the

therapist. In subsequent sessions, then, the therapist again focused on the patient but in a somewhat detached way. By the time the fourth or fifth relistening session arrived, few if any emotions were expressed on the part of the therapist. Thus the participant-gained impressions tended to fade, being replaced by observer-gained information. This was revealed by the fact that after the fifth session the opinions of the neutral observers and of the original participant tended to agree more than at the beginning, although there always remained some discrepancies which were probably due to the fact that the neutral observers never saw the patient but only heard him in action.

The systematic distortions which the various therapists showed seemed to constitute protective mechanisms used in interaction situations; they demonstrated the limitations of the observer capacity of a participant as well as the distorting influence of time on a past personal experience. It was found that these relistening experiments have an unusual effect on training in psychotherapy.

CONCEPT OF COMMUNICATION AND INTERACTION

Based on a review of the literature, as well as on our own observations and experiments, a comprehensive concept of the process of communication was developed. The structural components can be defined as follows:

The unit of consideration is always the total social situation with all its participants, regardless of whether or not they have communicated with each other. It is necessary to include in the study of communication all silent partners, because these essentially change the frame of reference of those persons who do communicate with each other.

Signs are necessary for communication. The semantic meaning of a symbol is taught to children in schools. However, because of the pragmatic components involved, different individual meanings are usually attributed to signs. For the understanding of a sign, the individual, after perception of the external cues, assigns within himself certain emotional values which may be termed "internal," or "proprioceptive," cues. This combination of external and internal cues transmits to him the individual meaning of the sign.

"Rules of the game" as defined by the culture govern any social situation. Regardless of whether the situation is defined as a game of bridge or chess, in which the rules are clearly outlined, or whether one deals with a burial or a marriage ceremony, in which some general directives are used, rules will govern the social interaction.

Stereotypes are images, prejudices or preconceived ideas about oneself, as well as about the other person. On the whole, one can say that the less personal contact and experience there has been the more

fixed the stereotype will be. Stereotypes are really the introjected parts of the other person which in fantasy interact with the stereotype of oneself.

The individual frame of reference one might call certain fixed premises and points of orientation which each participating person possesses for himself when entering into a social relationship, in order to help govern his own behavior.

The common frame of reference is developed when communication is achieved. Then one's own frame of reference is welded into a larger gestalt which contains all the factors previously listed as well as the frame of reference and other variables pertaining to and involving the other participating persons.

Individual processes necessary for communication are:

Knowledge of the motivation of each individual for entering into interaction, as well as of the goals which are to be achieved.

Understanding of self and the other is hence a process which precedes communication. It involves the subjective feeling of "fit" or comprehension one gets if various incomprehensible pieces are put together into a total gestalt, which then assumes meaning in terms of the systems in which a person thinks.

Once the individual has understood himself and the other, a necessary prerequisite to communication is self expression, which is used to convey to the other person the meaning that one attributes to exteroceptive as well as to proprioceptive cues. If this expression occurs in unison, then feelings, thoughts and actions all refer to and reflect the same focal point and express various aspects of one's relationship to a symbol (pragmatics). Expression in unison is easily understandable to the other person, while dissociation of thought, feelings and actions leads necessarily to a confusion of the partner. Neurotic and psychotic patients have difficulties in making themselves understood because they have difficulties in expression. These difficulties may be based either on the lack of familiarity with proprioceptive cues indicating interference, such as anger, anxiety, fear, shame, guilt and depression, or on lack of knowledge of proprioceptive cues pointing to needs for group membership, sex, hunger or thirst, or they may be based on the inability to coordinate externally perceived cues with existing proprioceptive cues. In psychotherapy, then, the patient-doctor relationship works toward a welding of these various isolated components of perception into a unit which can be used for the purpose of expression and thereby transmitted in understandable symbols.[12b]

Coordination of understanding as represented by factors related to perception and orientation of self and others in a total situation, with

action appropriate to this understanding, leads to successful interaction. If coordination does not occur, interaction is extremely difficult, if not impossible, as seen in certain schizophrenic reaction types.

The interaction processes which take place in the process of communication can be described as follows: Assuming that the participating persons want to communicate, that they possess the ability to express themselves, that they have perceived the frame of reference in which the social action takes place and that they also know the rules which govern this particular situation, each participant will make a preliminary survey of the other persons. In the Anglo-Saxon culture this approach technic [41] makes use of communization. At first, a common denominator is established by means of a documented mutual interest, whether it be in terms of comments regarding temperature, weather or some other safe topic. In this initial period of communization, a careful scrutiny of the other person is made in order to understand the other and to place this person consciously or unconsciously into one's own private system of personology. Tentatively, one's relation to the other person is clarified, possibly evaluated, and eventually steps are undertaken to continue communization, to part company or to proceed with communication.

In social gatherings long periods are frequently spent in clarifying definitions and the semantic meaning of certain signals. After these external barriers have been removed and a common denominator established in terms of acceptance of the meaning of certain external cues, the process of mutual understanding then proceeds to encompass the internal and proprioceptive cues associated by each individual to these external events. If the participants have understood each other, it means that they have been able to understand what kind of proprioceptive cues the other person has associated with the externally perceived signal. This, then, creates a common frame of reference, and once it has been established—that is, mutual understanding has taken place—the behavior of the participating persons may or may not be adjusted to this perceived frame of reference. Understanding—that is, the assessment of one's own frame of reference, comprehension of other person's frame of reference and welding the two frames of reference into a larger gestalt—has to be followed by appropriate action. There are, however, people who can never appreciate consequences of what originated within themselves. They perceive the reality situation but cannot follow through to the necessary consequences. Although in such a case communication is possible, it will not lead to successful interaction or to a gratifying relationship.

Panics, which are based on forced and infectious participation of a multitude of people, can be understood by considering the "feedback" mechanisms in communication. If person A is anxious and through

such behavior elicits a response in person B, this response, in turn, will either perpetuate or modify the behavior of A. Perpetuation of anxiety is likely to occur in person A if infection of person B is successful. This mutual reenforcement gradually leads to a snowball-like magnification of anxiety, and the ever-increasing excitation continues until a breaking point is reached at which a forced and usually irrational release is found, resulting in panic and stampede. Such a result can be prevented by alternate means: control and communication. In the case of control, the infected person B conceals his own excitation. At first such a procedure usually succeeds in attenuating the anxiety of person A, but sooner or later signs of anxiety will leak through, which when perceived by A will get the snowball rolling.

The most successful method for handling anxiety consists in sharing through communication. If person A is anxious and person B responds by objectively questioning with an attempt at understanding the anxiety of A as to its reasons and if consequently B remains calm because there is no reason for B to be alarmed, a progressive reduction of anxiety occurs in person A. Basic to this process is, of course, the ability of B to express himself, to understand and to communicate to A. If both persons possess the means of successful communication, anxiety arising in one person can be shared with others through cooperation in the removal of the cause of this anxiety.

SUMMARY

Pertaining to the therapeutic situation, a number of observations and experiments concerned with communication and interpersonal management of anxiety have been presented in this paper. From a theoretic viewpoint it is concluded that anxiety is initiated through the concomitant operation of several factors. Predetermined within a certain range is the organism's tolerance for excitation; intensity, sudden increments and rapid repetition of stimulation can produce anxiety and lead to disorganization of behavior. In addition, any stimulus when repeated assumes a certain cue value. A cue which in the past was associated with a threatening situation can initiate an alarm reaction. The organism then anticipates a repetition of danger experienced in the past. Furthermore, through assessment of the gestalt of a social situation, which includes the observer as an integral participant, impressions of fit, closure and familiarity will result in appropriate action, while impressions of nonfit and strangeness will be received with suspicion and may result in an alarm reaction.

In human beings transmission of anxiety occurs primarily through verbal and visual channels. Deviations in frequency, timing and intensity of the human voice betray acoustically the presence of anxiety, while visual observation may reveal additional signs of uneasiness.

Understanding of the verbal content, shifts in the type of words used or confusion and lack of understanding are further clues in the detection of anxiety. But beyond the simple issue of transmission, anxiety presents a particular problem because as it is infectious and can force active participation of originally uninvolved and neutral observers, as in the experiment described in which an audience was rendered anxious merely by listening to recorded interviews in which patients transmitted signs of anxiety.

The interaction taking place in successful communication can be conceived of as follows: In successive steps there are clarification of one's own frame of reference, understanding of the other person's frame of reference, mutual understanding and one-sided adjustment to the understood situation, followed by mutual adjustment. From various experiments it is concluded that the process of communication is essential for healthy functioning so that people may combine efforts to cooperate, complement and increase their ability to cope with animate and inanimate surroundings. The successful management of anxiety generated in daily life seems possible only through the process of sharing and communication. Alleviation of anxiety through personal contact is the process which is basic to all interpersonal relations from babyhood to old age. The ability to communicate and hence to share anxiety seems to constitute that process responsible for feelings of personal security of the individual. In psychotherapy, then, an attempt is made to further those processes which enable the patient successfully to manage his anxiety. As the principal psychotherapeutic tool for alleviation of anxiety this communication can then be utilized in other interpersonal relationships.

"THE BORDERLAND OF EPILEPSY"

A Reconsideration

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UNDER the title "The Borderland of Epilepsy," Gowers [1] in 1907 focused attention on a group of patients with fainting spells, vagal and vasovagal attacks, vertigo and similar episodic disturbances. He emphasized the difficulty in many instances of deciding whether or not the spells were epileptic and warned that even when such episodes are accompanied with loss of consciousness "a single attack of this character does not justify a diagnosis of epilepsy with all its attendant concern and anxiety."

The introduction of electroencephalography has provided an important new technic in the investigation of epileptic disorders, and the method helps to differentiate episodic phenomena that are primarily cerebral in origin from those which are extracerebral.

It has been demonstrated by Levin, Katz and Greenblatt [2] that for patients subject to typical "fainting spells" the incidence of electroencephalographic abnormalities is about the same as that for normal controls. On the other hand, about 90 to 95 per cent of patients with clinical epilepsy have interseizure electroencephalographic abnormalities.[3]

The present report deals with a series of 66 patients who had a history of at least one, but not more than three, convulsive episodes during their lifetime, and all of them had definitely abnormal electroencephalograms.

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1. Gowers, R. W.: The Borderland of Epilepsy: Faints, Vagal Attacks, Vertigo, Migraine, Sleep Symptoms and Their Treatment, London, J. & A. Churchill, Inc. 1907.

2. Levin, S.; Katz, J., and Greenblatt, M.: An Electroencephalographic Study of Cases with Syncope and Related Disorders, Am. J. Psychiat. **102:** 301-304, 1945.

3. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Classification of Epileptic Patients and Control Subjects, Arch. Neurol. & Psychiat. **50:** 111-128 (Aug.) 1943. Jasper, H. H., and Kershman, J.: Electroencephalographic Classification of the Epilepsies, ibid. **45:** 903-943 (June) 1941; The Value of Electroencephalography in the Diagnosis of Post-Traumatic and Others Forms of Epilepsy, Proceedings of the Fifth Meeting of the Associate Committee on Medical Research, Report no. C.6123, N. R. C., Canada, 1944.

MATERIALS AND METHODS

The patients were members of the Canadian armed services, and 85 per cent were between the ages of 18 to 30 years. Over 90 per cent were men, and they were all healthy and free from any other organic disease. All those who were subsequently found to have any definite cerebral or neurologic lesion were excluded. Patients whose seizures, however slight, could be recognized as focal in origin, or who had a clear focal electroencephalographic abnormality, were also excluded, as this focality was considered to be evidence of a localized cerebral lesion, even though its character and cause were not known. In the group there were an equal number who had had one, two or three convulsions. Patients with syncopal attacks who had a definite history of at least one convulsion were included in the group studied if their electroencephalogram was definitely pathologic.

The method used for electroencephalographic examination has been described elsewhere.[4] Patients with only borderline abnormalities were reexamined under hydration and administration of beta-hypophamine (pitressin®), using the regimen outlined by Penfield and Erickson.[5] In many instances in which there was a

Electrocephalographic Abnormalities in Patients with a History of Not More Than Three Convulsions

Type of Electroencephalographic Abnormality	No.	Per Cent
Bilaterally synchronous disturbances	49	74
3/sec. wave and spike activity	22	33
3/sec. variants	7	11
6/sec. rhythms and variants	20	30
Diffuse dysrhythmia	17	26
Total	66	100

history indicating that alcohol precipitated the seizure, the patient was given 1 ounce (30 cc.) of whisky in a glass of fruit juices three times at intervals of an hour, and the electroencephalogram was made about twenty minutes after the last drink.

ELECTROENCEPHALOGRAPHIC OBSERVATIONS

Analysis of the type of electroencephalographic abnormalities (table) shows that 75 per cent of the patients had bilaterally synchronous disturbances. The largest single group comprised 33 per cent who had 3 per second wave and spike patterns, closely followed by 30 per cent who showed bilaterally synchronous 6 per second rhythmic disturbances, including 4, 5 and 7 per second variants of this form of abnormality. A small group (11 per cent) showed variants of the 3 per second type of disturbance.

4. Jasper, H. H.; Kershman, J., and Elvidge, A. R.: Electroencephalographic Studies of Injury to the Head, Arch. Neurol. & Psychiat. **44:** 328-350 (Aug.) 1940.

5. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

The records of the remaining 26 per cent showed a diffuse dysrythmia. This was characterized by almost complete absence of the normal alpha frequency and its replacement by slow waves with a frequency varying from 2 to 6 per second. Usually, fast frequencies in varying amounts were mixed with these underlying slow waves.

CLINICAL CORRELATIONS AND ILLUSTRATIVE CASES

Three Per Second Wave and Spike Patterns (22 Patients).—Of the patients in this group, alcohol was known to be a specific factor producing the seizure in 10, and in 5 of them this postalcoholic seizure, occurring between four and eighteen hours after the spree, was the only one in their life history. The electroencephalographic abnormality in some instances was difficult to detect unless hyperventilation, hydration or alcohol itself was used. In sensitive patients a relatively small amount of alcohol could produce a considerable amount of pathologic activity, but the effect usually disappeared after twenty-four hours. In other patients fatigue was a frequent factor. Usually, there was no aura, and the attack was begun with sudden loss of consciousness followed by tonic and clonic movements.

The first patient, J. M., aged 22, a sergeant in the Royal Air Force, was a transport command navigator employed in ferrying aircraft and personnel between Montreal and India. After one very trying trip he was tired, and next evening he and a comrade went on a spree, consuming large amounts of whisky (rye), gin and beer. He had very little food. After sleeping only two hours, he was awakened by his friend, who was anxious to continue the spree. He went into the bathroom and started to shave, but does not recall anything further until he awakened in the hospital. His friend stated that he suddenly fell to the floor with generalized twitching of the arms and legs and frothing at the mouth. There was no incontinence or tongue biting. The patient had no history of previous convulsions, fainting spells, lapses of memory or absences, and there was no abnormality in the family history. Until the episode here described, he had seldom used much alcohol.

The first electroencephalographic examination, the day after the seizure, gave normal results with the patient at rest and during hyperventilation. The second, which was made immediately after forty-eight hours of hydration (fig. 1), showed a burst of typical 3 per second spike and slow wave activity, lasting four and a half seconds and not accompanied with any clinical changes. There was no change with hyperventilation. A repeat examination next day showed a few transient bursts of this abnormality at rest, but with one and a half minutes of hyperventilation a paroxysmal discharge lasting four and a half seconds occurred. These discharges were all primarily bifrontal with spread to other regions in the longer bursts. Three days later the patient was given 1 ounce of whisky in a glass of orange juice three times at intervals of one hour and the electroencephalographic examination repeated immediately after the last dose. This record showed frequent 3 per second spike and slow wave discharges at rest, with a pronounced increase during hyperventilation and afterward. The next day the electroencephalogram taken during rest was normal, and after three minutes of hyperventilation the

only irregularity was a transient burst of 6 per second waves with a spike, lasting about one second (fig. 1). The background alpha activity was normal.

A similar case is that of R. L. D., aged 21. On the night of his discharge from the army (May 1946) he went out celebrating with his friends and spent most of the night drinking steadily. In the next morning, before breakfast, he had a seizure which was described by his friend as "a sudden loss of consciousness with generalized shivering." There was no incontinence or tongue biting. The patient recalled feeling weak with a hang-over but remembered nothing of the spell. There was no family history of epilepsy, but several months before this episode the patient had what was described as a "nervous seizure" after a few successive nights of fairly heavy drinking.

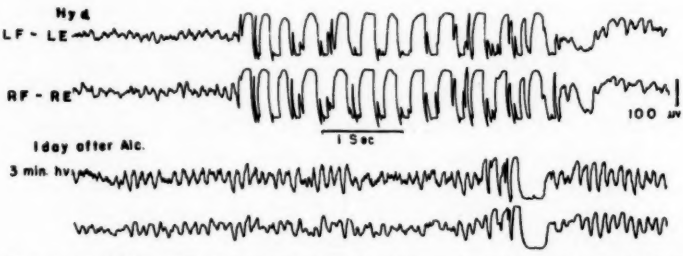

Fig. 1 (J. M.).—*Hyd* is the record taken during hydration and administration of beta-hypophamine (pitressin®); *LF-LE* is the left frontal region–left ear record, and *RF-RE*, the record from the homologous region on the right side, showing bisynchronous 3 per second wave and spike patterns. The lower two lines, taken one day after a test dose of alcohol, show the only recorded abnormality occurring after three minutes of hyperventilation.

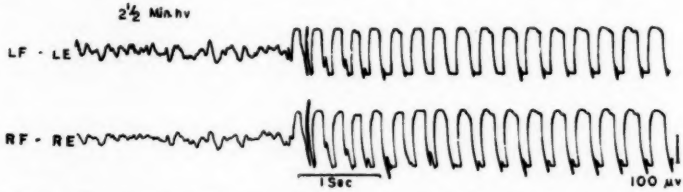

Fig. 2 (R. L. D.).—Three per second bisynchronous wave and spike patterns, occurring after two and a half minutes of hyperventilation, in the frontal region–ear records from the right and left sides.

Two electroencephalographic records taken after his first "nervous seizure" had been inconclusive. A third was taken after his last attack. The resting record was within normal limits, showing only occasional low voltage slow waves in the frontal regions. After two and a half minutes of hyperventilation, a typical burst of 3 per second spike and slow wave activity occurred (fig. 2), starting in the frontal regions. This lasted eight seconds and was not accompanied with any subjective or objective changes in the patient. Two shorter bursts and one of eight seconds occurred at three minutes of overbreathing. The posthyperventilation record was normal.

Bilateral Six Per Second Disturbances (20 patients).—There was often a history of minor episodes consisting of nausea, headache and

vomiting, and described as "biliousness." Syncopal spells and dizzy spells were much more frequent than in the group with 3 per second abnormality.

W. G. P. had had two fainting spells during treatment for minor bruises in a doctor's office, and one day, while at a blood donor clinic, he had a generalized convulsion after 50 cc. of blood had been withdrawn. This was the only convulsion in his life. His electroencephalogram (fig. 3) showed a moderately well regulated alpha rhythm with only occasional slow waves at rest. After one and a quarter minutes of hyperventilation, paroxysmal high voltage 3 to 6 per second waves appeared with occasional sharp waves. These abnormalities persisted for several minutes after the end of overbreathing. Reexamination after he had taken 75 Gm. of sugar in orange juice gave the same response.

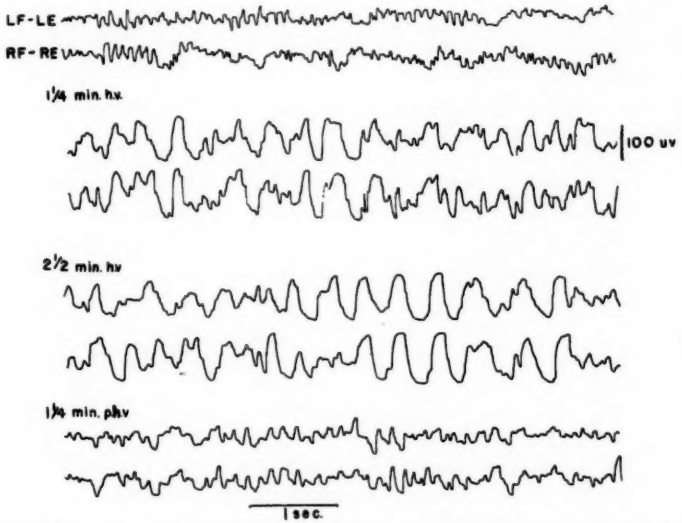

Fig. 3 (W. G. P.).—*LF-LE* is the frontal area–left ear record from the left side; *RF-RE* is the homologous record from the right side. At one and a quarter minutes of hyperventilation, high voltage slow waves occurred, which at two and a half minutes were continuous and at times rhythmic and bisynchronous. At one and a quarter minutes after the end of overbreathing (p. h. v.) there was still a considerable amount of 6 per second activity, although it was lower in voltage.

R. McK., aged 24, had four spells of loss of consciousness, with convulsive movements occurring only in the first and last attacks. The last spell was preceded by nausea and was followed by vomiting and a period of confusion lasting about one and a half hours. He complained of having had frequent "bilious spells" since childhood with "headache, nausea, vomiting and distorted vision." His electroencephalogram (fig. 4) showed periodic bursts of 5 to 6 per second waves in the frontal regions. This activity increased markedly during hyperventilation and was still present almost continuously one and a half minutes later.

Diffuse Dysrhythmias (17 Patients).—The records sometimes also showed bilaterally synchronous patterns. Alcohol was infrequent as a precipitating factor, but fatigue and emotional and physical stress were often present, and there was frequently a history of minor spells of dizziness or blankness.

D. H. P. was a 19 year old airman who was referred because of two convulsions which followed rather severe physical exertion and tiredness. Each started with a cry, the patient fell to the ground, and there were clonic movements of both arms and legs. There was no incontinence, but there was a period

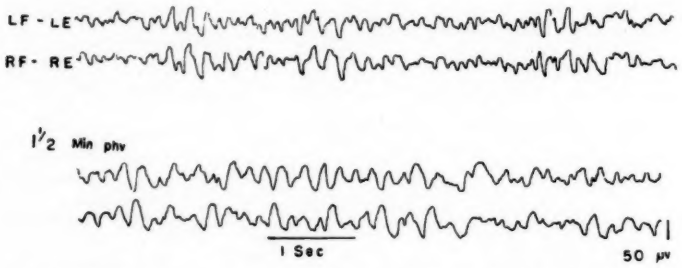

Fig. 4 (R. McK.).—*LF-LE* and *RF-RE* are the left frontal area–left ear and right frontal area–right ear records, respectively. At rest (upper two lines) there was a considerable amount of 6 second activity, which increased considerably during hyperventilation and was still pronounced one and a half minutes after the end of hyperventilation (p. h. v.).

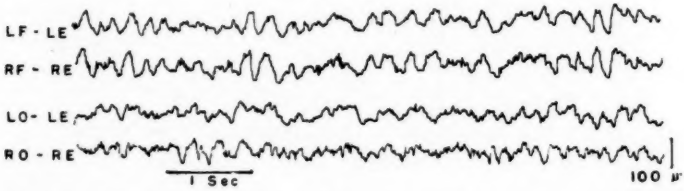

Fig. 5 (D. H. P.).—*LF-LE* the left frontal area–left ear record, and *RF-RE*, the homologous record from the right side. *LO-LE* is the left occiput–left ear record; *RO-RE* is the homologous record from the right side. The record shows a gross slow dysrhythmia, with little or no evidence of normal alpha frequencies.

of confusion lasting about ten minutes after the seizures. Except for occasional dizziness, his past and family histories were without significance. His electroencephalogram (fig. 5) showed practically no normal alpha activity. There was diffuse dysrhythmia with generalized slow activity and a tendency at times toward the formation of rhythmic slow waves.

Patients in this group were much more likely to have fainting spells than those with other electroencephalographic abnormalities. A series of 114 patients with diffuse dysrhythmia as the predominant elec-

troencephalographic abnormality and syncopal seizures as the major clinical manifestations has recently been reported elsewhere.[6]

COMMENT

From the pattern of the attacks in this series of patients and the form of the electroencephalographic abnormality, there is apparently a relation to idiopathic epilepsy, but the infrequency of the spells makes this diagnosis unwarranted.

Similar electroencephalographic abnormalities have been seen in patients subject to convulsions during eclampsia [7] and anesthesia [8] and in diabetic patients prone to have severe insulin reactions.[9] In these instances, as in many of the patients reported here, although the electroencephalographic abnormality was present, some specific stimulus or toxic agent precipitated the clinical seizure. A similar sensitivity to such stimuli as alcohol, fatigue and stress is also found in many patients with symptomatic epilepsy and a focal cortical lesion, and these factors may precipitate a clinical convulsion in a patient who is otherwise free from seizures. The exact relation between the electroencephalographic abnormality and the actual seizure is not known in either group, although the electroencephalographic discharges usually increase greatly before or during an attack.

Electroencephalographic abnormalities like those seen in cases of clinical epilepsy have also been found with a wide variety of conditions without convulsions, such as behavioral problems in children, psychopathic personalities and even certain types of psychoneurosis. This has led to the use of such terms as "epileptic equivalents" and "epileptoid" patients and various authors have identified these conditions with the patients described by Gowers in the "Borderline of Epilepsy."

It is necessary, however, to reread the case records cited by Gowers in 1907 [1] in the light of what has since then been learned about cerebral physiology. Penfield and co-workers [10] have demonstrated that certain types of vertiginous attacks, ictal and postictal automatisms and seizures preceded or accompanied with visceral sensations may be localized to specific cortical areas. Many of Gowers' cases fall into this group. There can be no doubt that such episodic clinical disturbances, even of

6. Kershman, J.: Syncope and Seizures, J. Neurol., Neurosurg. & Psychiat. **12**:25, 1949.

7. Rosenbaum, M., and Maltby, G. L.: Cerebral Dysrhythmia in Relation to Eclampsia, Arch. Neurol. & Psychiat. **49**: 204-213 (Feb.) 1943.

8. Williams, D., and Sweet, W. H.: The Constitutional Factor in Anaesthetic Convulsions, Lancet **2**: 430-433, 1944.

9. Greenblatt, M.; Murray, J., and Root, H. F.: Electroencephalographical Studies in Diabetes Mellitus, New England J. Med. **234**: 119-121, 1946.

10. Penfield and Erickson.[5] Penfield, W., and Jasper, H. H.: Highest Level Seizures, A. Research Nerv. & Ment. Dis., Proc. (1946) **26**:252-271, 1947.

a minor character, accompanied with manifestations of localized abnormal cortical discharge in the electroencephalogram should be classified as focal cerebral seizures.

If these cases are excluded, a group of patients remain in the "borderland of epilepsy" who have rare convulsive episodes and fainting spells and who show an abnormal electroencephalogram similar to that seen in idiopathic epilepsy. It is questionable whether the term "epilepsy" or its adjectives should be so broadened as to include other kinds of patients without convulsions but with similar electroencephalographic abnormalities. It is not clear how the electroencephalographic abnormalities of these patients are related to the underlying clinical disorder, and further investigation of this relation is essential. Epilepsy is a clinical meaningful term (referring to a group of symptoms with which everyone is familiar), and its use should be restricted to a definite clinical entity.

To avoid this apparent confusion, the term "cerebral dysrhythmia" was proposed by Gibbs, Gibbs and Lennox.[11] This term would be adequate for the "epileptoid" patients, or those with "epileptic equivalents" and abnormal electroencephalograms; but when applied specifically to the patients reported here with infrequent convulsions, it seems inappropriate mainly because dysrhythmias occur so commonly without convulsive seizures.

The use of the term "latent" epilepsy was advanced by Williams[12] and Weinberg,[13] in contrast to "active" epilepsy, but Williams concluded that such a broadening of the meaning of epilepsy was unwarranted. "Subclinical" epilepsy has also been used to describe the condition in this group, but it is open to the same criticism. Unfortunately, the term epilepsy carries with it important personal, social and occupational consequences, and it seems unfair to apply it unless there is indisputable justification.

"Cerebral syncope," or "encephalosyncope," has been proposed. Objections to the use of the word "syncope" have been raised because, as a result of usage, this term has become associated with clinical changes primarily due to vascular disturbances. However, this is not true by strict definition and origin of the word. Since syncope may be complicated by the appearance of a convulsion, and "cerebral syncope," or "encephalosyncope," suggests a primarily cerebral origin, this term might be an appropriate one. The alternative description of "larval or subclinical cerebral seizures" is suggested.

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11. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Epilepsy: A Paroxysmal Cerebral Dysrhythmia, Brain **60**:377-388, 1937.

12. Williams, D.: The Nature of Transient Outbursts in the Electroencephalogram of Epileptic Patients, Brain **67**:10-37, 1944.

13. Weinberg, M. H.: Fatigue As a Precipitative Factor in Latent Epilepsy, J. Nerv. & Ment. Dis. **101**: 251-256, 1945.

Whatever term is used, it is obvious that if the seizures become more frequent the diagnosis of idiopathic epilepsy becomes inevitable.

SUMMARY AND CONCLUSIONS

A group of 66 patients are described who had had only one, two or three convulsions in their lifetime.

Clinically and electroencephalographically they fell into three groups:

1. Patients with bilaterally synchronous 3 per second wave and spike abnormality in the electrocephalogram and a history that the clinical seizure was frequently associated with excessive alcoholic intake. There was no aura, and the attack was usually a major one.

2. Patients with a diffuse dysrhythmia in the electroencephalogram and a history that the seizures were precipitated by fatigue and emotional and physical stress. Frequently there were minor spells consisting of "dizziness," "blankness" and "fainting."

3. Patients with bilaterally synchronous 6 per second activity in the electroencephalogram and a history that the seizures were often associated with stress and preceded by nausea, vomiting, biliousness, etc.

3. These patients form a group which represents the "borderland of epilepsy," and their relation to the cases described by Gowers [1] is discussed.

4. There is need of a clinical diagnostic term for this group. This should appropriately describe the rare occurrence of seizures usually only in special circumstances. The terms "encephalosyncope" and "larval cerebral seizures" are suggested.

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PREFRONTAL LOBECTOMY IN SCHIZOPHRENIA

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MINNEAPOLIS

FRONTAL lobe surgery for mental disorders was started at the University of Minnesota in 1940. At that time a new form of psychosurgery, termed prefrontal lobectomy in keeping with present day terminology, was introduced.

Excision of the frontal areas was performed on each hemisphere in a coronal plane which passes just anterior to the anterior horn of the lateral ventricle. It seemed that by this excision under direct vision a more consistent and exact operation could be performed. It was also hoped that by modifying the excisions it would eventually be possible to determine what areas of the brain would have to be removed in the treatment of certain specific personality aberrations.

TECHNIC OF OPERATION

This operation has now been performed on 53 patients. At first these excisions were performed in two operations, the anterior part of only one hemisphere being excised at each of these operations. But when it was noted that the postoperative reaction following these unilateral excisions was relatively mild, the operation was extended to bilateral excision in one operation. The first 5 patients were operated on with the two stage technic, but subsequently the one stage operation has been consistently employed in all cases except 1. In this patient excision of the frontal areas of only the right hemisphere has been done because during their excision a large branch of the right anterior cerebral artery was accidentally ruptured, with hemorrhage and consequent technical difficulties, so that the operation was terminated as a unilateral excision. This patient will be referred to again in the discussion of results.

Read at the first International Conference on Psychosurgery, Lisbon, Portugal, Aug. 5, 1948.

From the Department of Surgery, Division of Neurosurgery (Dr. Peyton) and the Department of Psychiatry, University of Minnesota.

The operation consists in making a coronal incision in the scalp just anterior to the coronal suture and reflecting the anterior segment of scalp over the forehead. Bilateral frontal osteoplastic flaps are then reflected on the temporal muscle of each side similar to those made for transfrontal craniotomy for operations on the frontal lobe or parasellar region. Excision of the lobe is made in a coronal plane which passes through the posterior margin of the lateral part of the lesser wing of the sphenoid bone.

Blood vessels along the line of excision are occluded with silver clips or sutures. Cautery is not used, in order that its destructive effect on the remaining cerebral tissue may be avoided. The section of the hemisphere usually passes in front of the lateral ventricle, but occasionally the anteriormost part of the ventricle is entered. This has made no appreciable variation in the postoperative course of these patients. Section of the hemisphere is made with a sharp knife for the most part, but in the region of the anterior cerebral artery and its major branches a blunt instrument is used.

In the 53 cases in which this operation was done there were 3 postoperative deaths; all 3 were in the first 18 cases. One death was due to bilateral occlusion of the anterior cerebral arteries; another, to infection (meningitis), and the cause of death of the third patient, who died twenty-four hours after operation, is unknown.

The results in the first 15 patients operated on have been previously reported.[1] In this report the clinical effects of this procedure on a group of 32 patients with chronic schizophrenia will be reported.

MATERIAL

The 32 cases reported were selected from those of a group of the most severely disturbed patients in the Anoka State Hospital of Minnesota. This hospital has approximately 1,400 inmates. The characteristics of the group selected for operation were these.

1. The average age was 37 years, and the range was 27 to 45 years.

2. The psychiatric diagnosis was definitely schizophrenia according to accepted standards, and all subgroups of schizophrenia were represented. No case was included in which there was any evidence of organic brain disease.

3. The average duration of known psychosis was fifteen years and ranged from six to twenty-four years. The average duration of continuous hospitalization was twelve years and ranged from six to twenty-one years.

4. The prognosis in every case appeared to be hopeless, since there had been little or no evidence of improvement during the course of institutionalization.

5. Institutional adjustment of the group was exceptionally poor, as one might expect, since they were chosen from a group selected by the hospital personnel as presenting the most difficult problems of management among the entire hospital population. They were, as a rule, assaultive and disturbed and presented difficult feeding and nursing problems.

6. None of these 32 patients had ever received any form of shock therapy.

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1. Peyton, W. T.; Noran, H. H., and Miller, E. W.: Prefrontal Lobectomy: Excision of the Anterior Areas of the Cerebrum, Am. J. Psychiat. **104**:513, 1948.

7. In order to obtain frontal lobe specimens most suitable for neuropathologic study and especially to determine the neuropathologic changes due to electric shock therapy, the patients selected for this operation were those who had not suffered any disease or received any therapy that might have produced pathologic changes in the central nervous system.

MANNER IN WHICH MATERIAL WAS STUDIED

Each case was studied in the following manner: Composite histories were assembled from the records of all the various hospitals in which the patient had been previously confined, and this was supplemented by the patient's present symptomatology and progress as obtained from the Anoka State Hospital records and the observations made by the personnel of that hospital. When indicated, additional information was obtained by personal interview with the family or other informants.

Prior to operation, careful observations of behavior in the ward, at work and during recreation were recorded, and a survey of the mental status of each patient, including a characteristic sample of his discourse, was also recorded. Formal psychologic testing was not attempted because the patients selected for this operation were unable to cooperate in these procedures.

Before operation a complete physical and neurologic examination was done on each patient; a blood count, urinalysis and roentgenogram of the chest were made. On the majority, the spinal fluid was examined.

The patients thus chosen were arbitrarily divided into two groups. One group, consisting of 18 patients, were operated on without receiving any previous shock therapy. The other group (14 patients) were given a course of electric convulsion shock therapy, consisting of fourteen treatments which resulted in grand mal seizures. The voltage was 110, and the range of current was 300 to 700 milliamperes for 0.2 second. No preshock medication, such as administration of sedatives or curare, was given. The interval between shock treatment and frontal lobectomy varied from one to six months. One month after shock therapy the patients were completely reevaluated to determine the effect of this therapy.

All patients were transferred to the University Hospital for lobectomy and remained there for approximately ten days after operation, when they were returned to the Anoka State Hospital and placed in the ward which they had previously occupied. Arrangements were made that they should receive no special care or attention but that they should return to the same routine that they were on before operation. The privilege of visitors or home visits and paroles at the request of their family remained the same as that for all patients in this hospital.

The postoperative evaluation of these 32 schizophrenic patients, like the preoperative evaluation, was made for the most part through clinical observation and, as previously stated, in the same environment to which they had been accustomed for many years in the state hospital.

These patients have now been under observation eight to thirty-six months since operation (average fifteen months).[2] The neurologic examination was repeated, and a reevaluation of the mental status was done with special inquiry concerning specific features for comparison with the preoperative status.

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2. The average weight of tissue removed by bilateral lobectomy in these 32 cases was 108 Gm. and the range 70 to 135 Gm.

The following characteristics were especially observed, and the extent to which they were present before treatment, after shock therapy and after lobectomy was tabulated: assaultiveness; self assaultiveness; soiling; neglect of personal care in grooming, eating and bathing; abnormal motor acts; negative relationship with associates; abnormal discourse, and abnormal mental content.

RESULTS

The results of this survey are tablulated graphically in chart 1 for those receiving shock therapy and in chart 2 for the whole group.

Before operation 20 patients (63 per cent) were severely assaultive, 10 (31 per cent) were mildly assaultive and 2 (6 per cent) were not assaultive. Of the 20 severely assaultive patients, 15 became nonassaul-

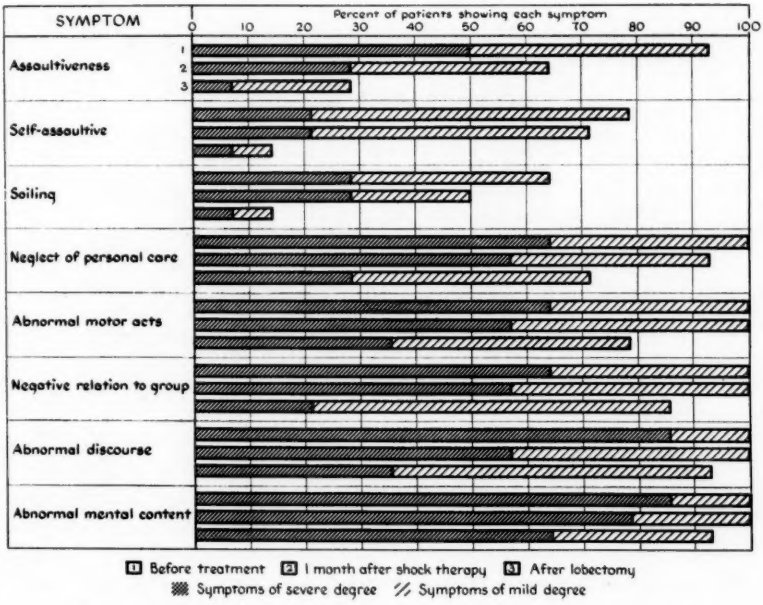

Chart 1.—Regressive symptoms before and after treatment in 14 patients.

tive, 2 remained mildly assaultive and 3 continued to be severely assaultive. Six of those mildly assaultive became nonassaultive.

Before operation 17 (53 per cent) were severely self assaultive, 10 (31 per cent) were mildly so, and 5 (18 per cent) did not have this tendency. Of the 17 severely self assaultive patients, 11 became nonassaultive, 3 were rendered mildly so and 3 remained severely assaultive. Of the 10 patients who were mildly self assaultive, 9 became nonassaultive.

Before operation 16 (50 per cent) presented extremely difficult problems because of soiling with urine and feces, 6 (19 per cent) were partially controlled and 10 (31 per cent) did not soil. Of the 16 who were uncontrollable before operation, 9 became entirely controlled, 4 now soiled themselves only occasionally, but 3 continued to soil themselves constantly. Of 6 who occasionally soiled themselves before operation, 5 no longer did so.

Before operation 24 (75 per cent) were almost completely unable to care for themselves in dressing, bathing and eating; 8 (25 per cent) were able partially to care for themselves, but none were able to dress, bathe and eat without some assistance.

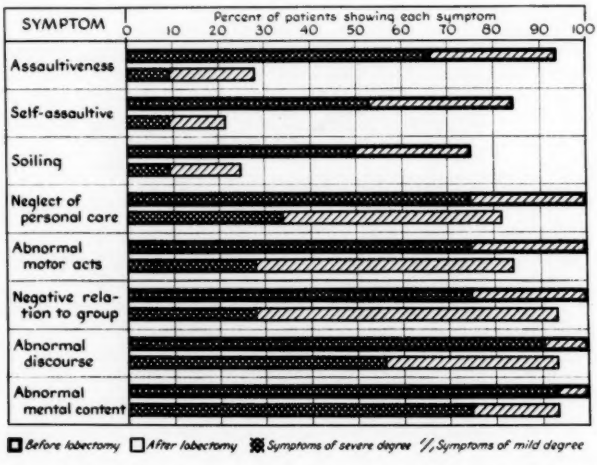

Chart 2.—Regressive symptoms before and after lobectomy in 32 patients.

Of the 24 completely unable to care for themselves, 3 became able to care for themselves without assistance and 13 became able to care for themselves partially; 8 were unchanged. Of the 8 who were able partially to care for themselves before operation, 3 no longer needed assistance, 4 remained unchanged and 1 became more helpless.

Under abnormal motor acts we include posturizing, catatonic positioning and other bizzare actions. Before operation, 24 patients (75 per cent) were characterized as severely abnormal in this category and 8 (25 per cent) mildly so. After operation, 4 previously classified as severely abnormal no longer performed abnormal motor acts; in 11 others this symptom became mild, but 9 were unchanged. Of the 8 who showed this symptom in mild degree before operation, 1 no longer performed abnormal motor acts but 7 were unchanged.

Of the 24 patients who showed negative relation to the group in severe degree before operation, 2 no longer showed this abnormality after operation and 14 related themselves better with the group; 8 were unchanged. In the 8 patients who showed this abnormality to mild degree before operation, there was no change following operation.

Of 29 patients whose discourse was extremely abnormal before operation, only 1 had his discourse changed to normal, 9 were improved but still were noticeably abnormal and 19 were unchanged. The discourse of 3 patients was mildly abnormal before operation; the discourse of 1 of these became normal after operation, and that of the other 2 was unchanged.

Mental content was grossly abnormal in 30 patients before operation. After operation no abnormality was demonstrable in 2 of them, mild

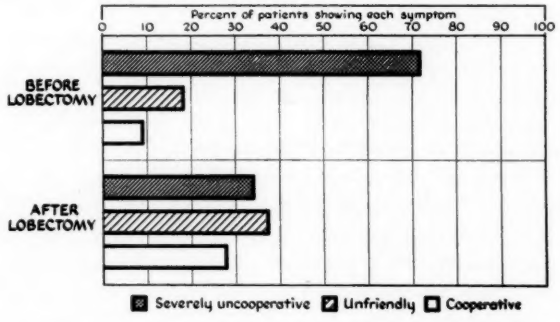

Chart 3.—Attitudes toward examiner before and after lobectomy in 32 patients.

abnormality persisted in 4 and 24 remained unchanged. Mental content was mildly abnormal in 2 patients before operation, and the contents remained the same after lobectomy.

An improved capacity for friendliness, cheerfulness and willingness to cooperate has been described as one of the more subtle changes in psychotic patients following surgical procedures on the frontal lobe.[3]

Capacity for friendliness was evaluated in our cases by willingness to remain in the room with the examiner, the patient's interest in the interview, apparent positive feelings toward the examiner and willingness to converse and follow simple directions. Chart 3 shows the results.

Before operation 23 patients (72 per cent) were completely indifferent to the examiner or overtly negativistic, 6 (19 per cent) were slightly cooperative and 3 (9 per cent) were friendly and cooperative.

3. Schrader, P. J., and Robinson, M. F.: Prefrontal Lobotomy: Evaluation Through Ward Behavior, J. Abnorm. & Social Psychol. **40**:61, 1945.

After lobectomy 9 (28 per cent) were cooperative, 12 (38 per cent) were slightly cooperative and 11 (33 per cent) remained indifferent or negativistic.

MISCELLANEOUS OBSERVATIONS

In only 1 patient was it noted that after operation there was a less active interest and ability to participate in institutional work and recreational activities; all others either had increased initiative in participation in these activities or remained approximately as they were before lobectomy.

During the presurgical work-up each patient was informed that he would undergo an operation on the brain for his illness. In case of the 15 patients who were given shock therapy, this announcement concerning a future operation was deferred until the shock therapy had been completed.

On reevaluation after lobectomy, the operation was again discussed with each patient and it was then found that 14 were so inaccessible that it was impossible to determine their comprehension or memory of anything related to the operation. Seventeen denied the possibility that any surgical procedures had been performed on them or that any major change had occurred in their regular institutional life, and they denied the existence of the craniotomy scars or had some ficticious explanation for them. Only 1 patient, with simple schizophrenia, recalled having had an operation and spontaneously alluded to it, but he was unable to recall any details of the events associated with it. Schrader [8] previously made similar observations after surgical procedures on the frontal lobe.

As a rule, these patients tended to follow a typical course after lobectomy, but there were exceptions. Those who were typical of the group, as a whole, had lost their aggressive and hostile behavior patterns when they returned to the state hospital after operation. Gradual change then occurred during the next three to six months, with a constant level of behavior acquired after eight months to one year following operative treatment.

Exceptions were as follows: Eight patients changed little for approximately three months, and then gradual changes began to appear. One patient, eventually classified as unchanged, was definitely less assaultive during the first year after operation and then gradually regressed to her preoperative status. One patient was improved after shock therapy but has not changed since operation. In 1 case, previously mentioned, only a right lobectomy was done because of technical difficulty. Immediately after operation there was monoplegia in the left lower extremity and the patient was severely ill, but she gradually recovered from the operative reaction over a six week period. This patient has made the most complete recovery of the entire group. She

is now home and is functioning at a normal level. One patient was isolated for pulmonary tuberculosis for six months after operation; during this period he received special attention and he gradually improved, but since isolation was terminated he has remained unchanged.

Three patients have not been improved by lobectomy. Two of these were unchanged, and the other has become an even more difficult problem in hospital management. This patient prior to lobectomy was restrained because of assaultiveness, destruction of clothing and occasional self assaultiveness. After operation there was some improvement in these symptoms for three months, but then she gradually became worse again until she was extremely vicious toward any one about her and so self assaultive that a collar had to be devised to prevent her biting accessible parts of her body.

LATE COMPLICATIONS

One patient has had grand mal seizures. Operation was done ten months ago; the first grand mal seizure occurred six months after operation, and three other seizures have occurred since. This patient changed from a preoperative state of apathy to the present state of extreme tension and excitability. Chronic osteomyelitis of a small part of the osteoplastic flap occurred in 2 cases, but in both there was prompt healing after removal of small fragments of necrotic bone.

PHYSIOLOGY

As a rule there was an increase in weight following lobectomy, but gain in weight and improvement in symptoms of schizophrenia were not well correlated. The 3 patients unchanged after operation gained an average of 18 pounds (8.2 Kg.), whereas 2 patients who lost weight, 3 and 38 pounds (1.3 and 17.2 Kg.) respectively, were definitely improved. On the other hand, the entire group of 19 patients who were very much improved gained an average of 15 pounds (6.8 Kg.) whereas the 8 patients only slightly improved gained an average of only 6 pounds (2.7 Kg.), but this difference is, at least in part, due to the fact that 2 of the much improved patients spent most of the first year after operation at home, where, probably because of better food and care, they gained an average of 47 pounds (21.3 Kg.).

GASTRIC MOTILITY AND GASTRIC SECRETION

Gastric emptying time was determined by giving a water and barium sulfate mixture by mouth and following its progress through the intestinal tract by fluoroscopy. This was done on 8 patients with

schizophrenia before lobectomy and again after they had recovered from the immediate postoperative reaction (approximately ten days after operation).

The gastric emptying time was not abnormal before operation and was not changed by lobectomy. Certainly the delayed emptying time observed after bilateral vagotomy did not follow lobectomy.

Gastric secretion before and after lobectomy was studied. Day and night specimens were collected by passing an intranasal gastric tube and connecting this to the Wangensteen siphon equipment. A daytime specimen was collected with this continuous suction from 9 a. m. to 9 p. m. and then continued another twelve hours, or until 9 a. m., for the collection of a night specimen. At the end of this twenty-four

Gastric Secretion

	Before Operation	After Operation
Free acid secretion, 17 patients		
Average day	13.6 units	15.2 units
Average night	13.1 units	15.2 units
Total acid secretion, 18 patients		
Average day	31.5 units	35 units
Average night	31.5 units	32.1 units
After 15 units of crystalline zinc insulin, 3 hours (hypoglycemia)		
Free acid, 16 patients (average)	23.0 units	19.4 units
Total acid, 18 patients (average)	35.0 units	39.1 units
Volume of gastric secretion, 16 patients		
Volume of gastric secretion		
Day volume (average)	538 cc.	448 cc.
Night volume (average)	362 cc.	351 cc.
Total 24 hours secretion	900 cc.	799 cc.
After 15 units crystalline zinc insulin (hypoglycemia)		
After 15 minutes, 19 patients (average)	18 cc.	18 cc.
After 3 hours, 19 patients (average)	120 cc.	117 cc.

hour period of continuous aspiration, crystalline zinc insulin injection (15 units) was administered intravenously and then additional specimens of gastric juice were collected every thirty minutes for three hours for acidity determinations. To carry out this test, these patients were without food by mouth for approximately forty-two hours, during which time they were sustained on fluids administered intravenously. The results of this study of gastric secretion are given in the accompanying table. There was no significant difference in the amount of gastric secretion or the gastric acidity after operation.

EFFECTS OF DRUGS

The effect of certain drugs on the blood pressure before and after lobectomy was investigated. No significant difference in response to these drugs was demonstrated. This is not similar to reported observations after prefrontal leukotomy.[4]

4. Reitman, F.: Autonomic Responses in Prefrontal Leucotomy, J. Ment. Sc. **91**:318, 1945.

Before and after lobectomy 8 patients were given 0.64 mg of atropine sulfate; 50 mg. of ephedrine and 0.5 mg. of neostigmine methylsulfate (prostigmin methylsulfate®) 1:4,000 were given to 7; 1.5 cc. of epinephrine hydrochloride (1:1,000) was given to 6 patients; 10 mg. of amphetamine sulfate (benzedrine sulfate®) was given to 5 patients, and 10 mg. of methacholine chloride (mecholyl chloride®) was given to 4 patients. All these drugs were given hypodermically both before and after lobectomy, and the blood pressure was recorded every fifteen minutes for two hours. Diphenhydramine hydrochloride (benadryl hydrochloride®), 50 mg., was given by mouth to 5 patients and similar blood pressure readings were recorded. There was no significant difference in the blood pressure response to any of these drugs after lobectomy.

PATHOLOGIC CHANGES

There has been much variation in the reported pathologic findings after shock therapy, both in experimental animals and in man.[5] Animal experiments have not been conclusive; in some experiments the dosage was much greater than that used therapeutically in man, and it has been found difficult to administer electric shock to animals that is exactly similar to the therapeutic treatment in man. Also the effects seem to vary with the species of experimental animal, probably because of differences in susceptibility.

Human material examined after shock therapy has been obtained from autopsy specimens, and some of the conditions described were possibly secondary to the terminal illness.[6] Some of these autopsy specimens were from old people, and it has been suggested that changes described might be, at least in part, those changes in the brain due to age.

As previously stated, 14 of the 32 patients reported on received shock therapy before lobectomy, the interval between shock and lobectomy varying between one and six months. None of these patients was over 45 years of age, and they were in good physical condition when the specimen was obtained.

Serial sections on all frontal lobes removed are being made and stained with Weil, Nissl and hematoxylin and eosin stains. At this time sections from only 8 patients, 4 of whom had and 4 of whom had not received electric shock therapy, have been studied. The variation

5. Will, O. A.; Rehfeldt, F. C., and Neumann, M. A.: A Fatality in Electroshock Therapy, J. Nerv. & Ment. Dis. **107**:105, 1948.

6. Ebaugh, E. G.; Barnacle, C. H., and Neuberger, K. Z.: Fatalities Following Electric Convulsive Therapy, Tr. Am. Neurol. A. **68**:36, 1942.

from normal is very slight and is the same in both those who received shock and those who did not. There was no gross abnormality, but microscopically throughout the lobes there were scattered nerve cells which were pyknotic and shrunken. This was not uniform in the various cases but was present to some degree in all.

COMMENT

These 32 cases of psychosis included 2 cases of simple schizophrenia, and the three other formal subdivisions of schizophrenia were approximately equally represented. But the patients were a rather homogeneous group, characterized by chronic illness (minimum six years); they were delusional, regressed and assaultive. The response of the different types to lobectomy was apparently similar; however, there were not enough cases of each type to permit drawing of any definite conclusions.

There was no correlation between the age of the patient and response to lobectomy, and it would appear that the duration of the psychosis had little prognostic significance in case of these patients with chronic psychosis subjected to lobectomy. The average duration of recognized psychosis was fifteen years. For the 21 patients who responded most favorably the average was 14.6 years; for 8 patients who responded less favorably the average was sixteen years, and for the 3 who were unchanged by operation the average duration of illness was eighteen years. We have done lobectomy on no patient with schizophrenia of less than two years' duration, for whom the prognosis of recovery after lobotomy is reported to be much better.[7]

Freeman and Watts [8] have stated that a favorable response to shock therapy is an indication that a favorable response will follow lobotomy. Our experience is, in general, somewhat similar. The 15 patients subjected to shock treatment were evaluated one month after this treatment. In general, the greatest response to shock was improvement in the symptoms of assaultiveness, self assaultiveness and soiling. This improvement was temporary, and as a rule in a few weeks the previous pattern of behavior reappeared. Improvement after shock therapy was much less evident or common in the other symptoms evaluated—that is, in neglect of personal care, abnormal motor acts, negative relationship with associates, abnormal discourse and abnormal mental content. The response to lobectomy was more pronounced than to shock therapy and it was more lasting, but most patients who responded to shock therapy got a better result after lobectomy than did those who did not react to shock therapy.

7. Scarff, J. E., and Kalinowsky, L. B.: Prefrontal Lobotomy Under Direct Vision, New York State J. Med. **47**:2669, 1947.

8. Freeman, W., and Watts, J. W.: Prefrontal Lobotomy: The Problem of Schizophrenia, Am. J. Psychiat. **101**:4, 1945.

SUMMARY AND CONCLUSIONS

The technic of a new frontal lobe operation for mental disorders is described. This operation consists in the bilateral excision of the cerebral tissue anterior to the site at which incision is made in frontal lobotomy. It has been performed on 53 patients.

The results obtained by this lobectomy in 32 cases of chronic schizophrenia are shown graphically and described in detail. The most striking results were obtained in the elimination or reduction of assaultiveness and in the elimination of soiling. Improvement in mental content was rare.

Fourteen of these 32 patients were given shock therapy preliminary to lobectomy. There was some correlation in the response to electric shock and to lobectomy. Those patients that improved after shock therapy were also more improved by lobectomy.

Only 3 of the 32 patients were not improved by lobectomy, and 1 of these has since operation become an even more difficult problem in hospital management.

Gastric motility and gastric secretion were found to be normal in these patients with schizophrenia and were not changed by operation.

The blood pressure response to drugs was not changed by lobectomy.

Gain in weight and improvement following operation were not correlated.

Minimal changes in cells were found scattered throughout the excised part of the frontal lobe. These cellular changes were the same when shock had been given, and no additional tissue abnormality was seen after shock therapy.

ASEPTIC HEMOGENIC MENINGITIS

An Experimental Study of Aseptic Meningeal Reactions Due to Blood and Its Breakdown Products

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HEMOGENIC meningitis is the name proposed for the aseptic meningitis due to blood usually occurring one to five days after a subarachnoid hemorrhage, which may follow intracranial operations, craniocerebral injuries or ruptured or leaking intracranial aneurysms. The purpose of this paper is to present experimental evidence that specific breakdown products of blood are responsible for the aseptic meningeal reactions and hyperthermia observed when blood is present in the subarachnoid space.

LITERATURE

1. *Clinical Review.*—The literature contains reports of aseptic meningeal irritation following spontaneous subarachnoid hemorrhage [1] and leaking or ruptured aneurysms.[2]

Mallory [3] reported a case of intracranial varicosities in which symptoms of meningeal irritation followed each episode of rupture. Such a clinical picture is not unlike that seen in patients with leaking aneurysms.[2b]

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

1. Lamb, F. H.: Spontaneous Meningeal Hemorrhage, J. Lab. & Clin. Med. **15**:531-538, 1930. Strauss, I.; Globus, J. H., and Ginsburg, S. W.: Spontaneous Subarachnoid Hemorrhage, Arch. Neurol. & Psychiat. **27**:1080-1132 (May) 1932. Bagley, C.: Spontaneous Cerebral Hemorrhage, ibid. **27**:1133-1174 (May) 1932. Cookson, H.: Spontaneous Subarachnoid Haemorrhage, Brit. M. J. **1**:555-558, 1933. Sands, I. J.: Subarachnoid Hemorrhage, Tr. Am. Neurol. A. **64**:144-151, 1938.

2. (*a*) Collier, J.: Observations on Cerebral Haemorrhage Due to Causes Other Than Arteriosclerosis, Brit. M. J. **2**:519-521, 1931. (*b*) Bramwell, E.: Upon Leaking Aneurysms of Cerebral Arteries as Cause of Third Nerve Paralysis, with Special Reference to Two Cases in Which Diagnosis Was Confirmed by Arterial Radiography: Note Upon Aetiology of Recurrent and Periodic Ocular Palsy and Ophthalmoplaegic Migraine, Tr. Ophth. Soc. U. Kingdom **54**:205-221, 1934. (*c*) Richardson, J. C., and Hyland, H. H.: Intracranial Aneurysms, Medicine **20**:1-83, 1941. (*d*) Dandy, W. E.: Intracranial Arterial Aneurysms, Ithaca, N. Y., Comstock Publishing Company, 1944.

3. Mallory, T.: Presentation of a Case, Case Records of the Massachusetts General Hospital, New England J. Med. **218**:529-531, 1938.

The cerebrospinal fluid is usually pink to xanthochromic, but may be colorless.[4]

Aseptic meningeal reactions are often seen following craniocerebral injuries. Spurling[5] stated that fresh blood acts as an irritant in the spinal fluid, but when red cells disintegrate, thus forming bilirubin and biliverdin, the irritative reaction is tremendously increased. The stiff neck and perhaps the elevation in temperature are due to the irritation of the decomposition products of hemoglobin. Russell[6] found that on the second or third day after injury the number of leukocytes in the spinal fluid may rise and be associated with signs and symptoms of meningeal irritation which subside in a few days.

Aseptic meningitis following intracranial operations has been frequently reported. Different authors have proposed different causes, although they all agree that the nature of this meningitis is noninfectious.

The intracranial epidermoids or cholesteatomas appear to be responsible for most of the literature on postoperative aseptic meningitis.[7] This complication has been occasionally reported following the removal of a cerebellar hemangioma,[8] meningioma,[9] craniopharyngioma[10] and cystic neoplasm.[11]

Of great concern to many neurosurgeons is a recurrent form of aseptic meningitis following certain intracranial procedures. Finlayson and Penfield,[12] who in 1941 first described this form of meningitis as a clinical entity, postulated that the cause is the presence of breakdown

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4. Bagley, C.: Functional and Organic Alterations Following the Introduction of Blood Into the Cerebrospinal Fluid, A. Research Nerv. & Ment. Dis., Proc. (1927) **8**:217-243, 1929. Bramwell.[2b]

5. Spurling, P. G.: Craniocerebral Trauma, in Bancroft, F. W., and Pilcher, C.: Surgical Treatment of the Nervous System, Philadelphia, J. B. Lippincott Company, 1946, pp. 33, 36 and 37.

6. Russell, R.: Discussion on the Diagnosis and Treatment of Acute Head Injuries, Proc. Roy. Soc. Med. **25**:751-757, 1932.

7. Bailey, P.: Further Observations on Pearly Tumors, Arch. Surg. **8**:524-534 (March) 1924. Critchley, M., and Ferguson, F. R.: The Cerebrospinal Epidermoids (Cholesteatomata), Brain **51**:334-384, 1928. Sachs, E.: The Diagnosis and Treatment of Brain Tumors, cited by Finlayson and Penfield,[12] p. 271. Kreig, W., cited by Finlayson and Penfield.[12] Olivecrona, H.: On Suprasellar Cholesteatomas, Brain **55**:122-134, 1932. Love, J. G., and Kernohan, J. W.: Dermoids and Epidermoid Tumors (Cholesteatomas) of the Central Nervous System, J. A. M. A. **107**:1876-1883 (Dec. 5) 1936.

8. Cushing, H., and Bailey, P.: Tumors Arising from the Blood Vessels of the Brain, Springfield, Ill., Charles C Thomas, Publisher, 1928, p. 110.

9. Olivecrona, H., cited by Finlayson and Penfield.[12]

10. Bailey, P.; Buchanan, D. N., and Bucy, P. C.: Intracranial Tumours in Childhood, Chicago, The University of Chicago Press, 1948, p. 368.

11. Merrem, G., cited by Finlayson and Penfield.[12]

12. Finlayson, A. I., and Penfield, W.: Acute Postoperative Aseptic Leptomeningitis, Arch. Neurol. & Psychiat. **46**:250-276 (Aug.) 1941.

products of a blood clot entering the subarachnoid space. They stated that after removal of a neoplasm or an atrophic epileptogenic lesion a blood clot is left behind which soon undergoes degeneration and liquefaction. The breakdown products of the blood clot accumulate and are discharged into the subarachnoid spaces, either indirectly through an opened ventricle in the case of supratentorial procedures or directly by way of the cisterna magna in the case of infratentorial procedures.

Sachs [13] stated that blood in the cerebrospinal fluid unquestionably causes an elevation in temperature and that it is particularly noticeable in posterior fossa operations in which some patients experience meningeal symptoms.

2. *Experimental and Pathologic Review.*—Within a few hours after the introduction of blood into the subarachnoid space of animals, there is an outpouring of polymorphonuclear leukocytes into the cerebrospinal fluid, reaching a maximum within twenty-four hours and then beginning to disappear.[14] The permeability of the meninges to the contents of the blood is increased by inflammation, and the polymorphonuclear cells invade an injured region by adhering to the endothelium of the dilated blood vessels and reaching the avascular arachnoid from the vascular pia.[15] These polymorphonuclear cells are found in the pia-arachnoid, the cerebral ventricles and the choroid plexuses.[15a] After irritation of the meninges is sustained, the perivascular space becomes filled with lymphocytes, which appear in the spinal fluid along with macrophages during the second twenty-four hours.[14b] As a result of irritation, the cells lining the space hypertrophy, lose their attachments and engage in removing the debris. Essick [14b] concluded that the reaction produced is due solely to physical contact with the arachnoid.

The soluble matter of the blood is promptly digested, and only the iron pigment remains.[16] Hassin further stated that these blood pigments

13. Sachs, E.: The Care of the Neurosurgical Patient, St. Louis, C. V. Mosby, 1945, pp. 246-247.

14. (*a*) Wegeforth, P.; Ayer, J. B., and Essick, C. R.: The Method of Obtaining Cerebrospinal Fluid by Puncture of the Cisterna Magna (Cistern Puncture), Am. J. M. Sc. **157**:789-797, 1919. (*b*) Essick, C.: Formation of Macrophages by the Cells Lining the Subarachnoid Cavity in Response to the Stimulus of Particulate Matter, Carnegie Institute of Washington Publications, Contrib. Embryol. **272**:379-388, 1929. (*c*) Ayer, J. B.: A Pathological Study of Experimental Meningitis from Subarachnoid Inoculation, Monograph of the Rockefeller Institute for Medical Research, no. 12, 1920, pp. 26-44.

15. (*a*) Flexner, S., and Amoss, H.: Localization of Virus of Epidemic Poliomyelitis, J. Exper. Med. **20**:249-268, 1914. (*b*) Kubie, L. S., and Schultz, G. M.: Vital and Supravital Studies of the Cells of the Cerebrospinal Fluid and of the Meninges in Cats, Bull. Johns Hopkins Hosp. **37**:91-129, 1925.

16. Hassin, G. B.; Isaacs, H., and Cottle, M.: Clinical Pathological Report of a Case of Pons Haemorrhage (Type Foville), J. Nerv. & Ment. Dis. **56**:553-561, 1922. Essick.[14b]

were found in the perivascular spaces, having been carried from the brain to the subarachnoid space just as any other useless foreign substance is removed from brain tissue. He reported studies of cerebral hemorrhage in which the subarachnoid space contained large numbers of macrophages filled with blood pigments.[17] Blood cells in the subarachnoid space are intermingled with histiocytes, fibroblasts, mesothelial cells and lymphocytes and, in long-standing cases, with newly formed proliferative connective tissue fibers. Hassin [18] reported that cells are often enclosed within macrophages or histiocytes which, like the fibroblasts, are packed with granules of blood pigment, while the scattered mesothelial cells, usually found in nests, do not exhibit any phagocytic activity but remain passive. These statements are contrary to those of Essick, who stated that there was a transition of the mesothelial cells into macrophages.

Bagley [19] reported similar pathologic observations with the addition that some of the meninges showed no thickening and appeared normal. The toxic clinical course of his animals continued for several weeks interrupted with intermittent intracisternal injections of fresh whole blood. The meninges were thickened and stained at the sites of contact with the blood in a few dogs that received cortical injections of autogenous blood. After the acute reaction subsided, a deposition of fibrous tissue with pigment-laden phagocytes was present. From these observations he suggested the possibility that such a pigment is the causative factor of the aseptic meningitis which follows the presence of blood in the subarachnoid space.

Hammes [20] studied necropsy material from 114 cases of subarachnoid hemorrhage in which there was no history of trauma, intracranial operation, or systemic disease and in which the rupture of a cerebral aneurysm was the source of bleeding. In 9 cases in which death was sudden, blood was most prominent about the base in the large cisterns, since this was the site of hemorrhage. Blood had diffused over the hemispheres and down the cord. The meninges were free of reaction. When death occurred one to four hours following rupture of the aneurysm, a small collection of polymorphonuclear cells was present around the pial blood vessels. When death occurred in four to sixteen hours, an increased reaction of polymorphonuclear cells was noted, with lymphocytes beginning to appear. A greater diffusion of polymorphonuclear cells and

17. Hassin, G. B.: The Effect of Organic Brain and Spinal Cord Changes on the Subarachnoid Space, Choroid Plexus, and the Cerebrospinal Fluid, A. Research Nerv. & Ment. Dis., Proc. (1924) **4**:368-394, 1926.

18. Hassin, G. B., in Brock, S.: Injuries of the Skull, Brain and Spinal Cord, Baltimore, Williams & Wilkins Company, 1943, pp. 27-28.

19. Bagley, C.: Blood in the Cerebrospinal Fluid: Experimental Data, Arch. Surg. **17**:18-38 (July) 1928. Footnote 4.

20. Hammes, E. M.: Reaction of the Meninges to Blood, Arch. Neurol. & Psychiat. **52**:505-514 (Dec.) 1944.

lymphocytes was found in the group that died sixteen to thirty-two hours after the initial onset, but the multinuclear cells were still predominant. After the first twenty-four hours, the mesothelial cells began to take part in the reaction. It was during this period that the first evidence of the breakdown products of blood was present in the form of brown pigment and iron, free and within the cytoplasm of the multinuclear cells, and leukocytes in the subarachnoid space. All cells increased in number when death occurred in three days. The multinuclear cells were now less than half of all cells present. The activity of phagocytes and mesothelial cells became more evident. The mesothelial cells were filled with red blood cells, pigment, iron and degenerated leukocytes. In some areas only polymorphonuclear cells were found, and in other areas, only lymphocytes. The polymorphonuclear reaction had subsided when death occurred in a week, but the pigment and iron were increased and intact red blood cells could still be seen. The first appearance of fibrosis of the meninges occurred in 50 per cent of patients who died ten days following rupture of the aneurysm. The pia was bound to the arachnoid and was patchy in character where blood was found to be in contact with the subarachnoid space. Phagocytes and lymphocytes were present as long as any breakdown products of blood were present.

EXPERIMENTAL STUDIES

This is a comparative study of aseptic meningeal reactions in dogs following intracisternal injections of blood and its breakdown products.

1. *Methods.*—All animals were observed for several weeks before the experiments. The cisternal punctures were carried out aseptically after intravenous injection of thiopental sodium (pentothal sodium®). As a rule, the animals had recovered from the anesthesia within fifteen to thirty minutes. Depending on the weight of the animal, usually 1 to 3 cc. of blood or its breakdown products was slowly introduced into the subarachnoid space. In all instances, 1 to 2 cc. more of cerebrospinal fluid was withdrawn than the amount introduced. After the subarachnoid injections, the animals were observed and examined hourly for the first seven hours and then several times a day for the following week. The spinal fluid was usually withdrawn five hours after the injection because the peak of the cellular reaction occurred at this time [14b,c] and complete admixture of cerebrospinal fluid and foreign material had taken place. The cellular response at the five hour interval was predominantly polymorphonuclear.

The normal temperature variation of dogs in our laboratories ranged between 99 and 102 F. Therefore, only degrees of temperature above 102 F. when present at the five hour interval will be considered evidence of pathologic pyrexia. The normal values for the total protein in the spinal fluid varied from 10 to 25 mg. per hundred cubic centimeters. Utmost precaution was taken at all times to keep the injected materials sterile.

2. *Material and Results.*—(*a*) Autogenous Fresh Whole Blood (table 1): This substance will serve as a base line for the other materials injected.

After the needle was placed into the cisterna magna, 2 cc. of blood [21] was withdrawn from the femoral vein and immediately injected into the subarachnoid space.

No clinical signs of meningeal irritation were observed in the 9 animals in this group. The cerebrospinal fluid recovered five hours after the injection revealed a mild cellular and protein response, as shown in table 1. Pleocytosis and xanthochromia were present as long as nine to twelve days after the injection. Two dogs experienced a slight elevation of temperature above 102 F. but were quite active and playful. The spinal fluid withdrawn the following day contained either an increase or about the same number of leukocytes as obtained at the five hour interval, but no signs of meningeal irritation or of pyrexia were present.

TABLE 1.—*Meningeal Response Five Hours Following Intracisternal Injection of Autogenous Whole Blood*

	Cerebrospinal Fluid			
Experiment No.	White Blood Cells, per Cu. Mm.	Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Clinical Signs of Meningitis
5	...	...	0.0	None
6	480	874	0.6	None
8	...	...	0.0	None
10	...	...	0.0	None
16	400	273	0.0	None
20	...	...	0.0	None
30	385	1,130	0.8	None
48	600	384	0.0	None
82	380	565	0.0	None

(*b*) Autogenous Whole Blood Incubated at Body Temperature for one to twelve Days (table 2): Autogenous blood was kept at body temperature from one to twelve days either in a test tube in an incubator or within a cellophane sac placed in the gluteal muscles of the animal. When the specimens were ready for injection, there was a firm clot with chocolate-colored supernatant fluid, which contained 1,000,000 to 2,000,000 degenerated red blood cells with a great deal of stroma, 15 to 20 Gm. of protein per hundred cubic centimeters and none of the spectroscopic bands seen in fresh blood.

Meningeal responses of varying degrees as shown in table 2 were obtained in the 12 dogs following the intracisternal injection of autogenous "degenerated" blood. Five hours after the injection of the one and two day old blood, there was noted a mild degree of malaise, pain in the neck on acute flexion (no pain is elicited normally when the

21. Blood contained between 8,000 and 9,000 leukocytes per cubic millimeter, 4,000,000 and 5,000,000 erythrocytes per cubic millimeter and 8 to 9 Gm. of serum protein per hundred cubic centimeters.

neck is acutely flexed), hyperthermia and a moderate cellular response in the spinal fluid. Severe aseptic meningitis followed the injection of the blood incubated three days or longer. The spinal fluid at the five hour interval appeared dark red and showed a pronounced cellular reaction averaging 3,759 leukocytes per cubic millimeter. Results of bacteriologic studies on several specimens were reported negative. The malaise and stiffness of the neck were so severe in 4 animals that they merely lay in their cage with their necks extended, making no attempt to sit up or eat for the remainder of the day and, in some instances, for the following day. There was no appreciable difference in the reactions from the blood incubated in the test tube [22] and from that in the cellophane sac in the

TABLE 2.—*Meningeal Response Five Hours Following Intracisternal Injection of Autogenous Blood Which Had Been Incubated at Body Temperature for One to Twelve Days (Degenerated Blood)*

		Cerebrospinal Fluid			Severity of Clinical Signs of Meningitis	
Experiment No.	Incubation, Days	White Blood Cells, per Cu. Mm.	Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Malaise	Stiffness of Neck
99	1	2,000	574	1.6	Mild	Mild
100	1	2,700	491	2.0	Mild	Mild
102	2	2,400	455	1.4	Mild	Mild
101	2	1,880	382	2.0	None	Mild
37	3	4,000	1,020	3.0	Severe	Severe
93	3	.....	.....	3.0	Severe	Moderate
41	4	4,400	600	3.2	Moderate	Severe
44	4	4,000	748	1.8	Moderate	Mild
27	7	4,500	750	3.8	Severe	Severe
29	7	1,800	812	2.8	Severe	Severe
45	8	3,740	969	2.0	Severe	Moderate
47	12	3,860	732	5.0	Severe	Severe

gluteal muscles. Five-tenths cubic centimeter of three day old degenerated blood was not a sufficient amount to produce meningeal reactions. However, if the spinal fluid contained an abnormal number of leukocytes as a result of a previous intracisternal injection of three day old degenerated blood, full-blown meningitis occurred. Such a response can best be explained on the basis that the meninges had not fully recovered from the first irritant and now only a smaller amount of toxic material was necessary to cause a severe meningeal reaction. When the same material [23] was introduced intracisternally two weeks apart, the reactions

22. As a control to the test tube method of incubation, autogenous cerebrospinal fluid was kept in an incubator at body temperature for five days and then injected intracisternally. Five hours later there was only a very mild cellular response in the cerebrospinal fluid; the temperature was not elevated, nor any clinical signs of meningeal irritation observed.

23. Autogenous incubated blood, autogenous fresh whole blood, autogenous hemolyzed red blood cells, autogenous incubated serum and bilirubin solutions.

observed following each injection were as reported in each group. In no instance would the responses obtained suggest an alteration of the sensitivity of the meninges due to these substances.

(*c*) Autogenous Plasma Incubated at Body Temperature for Four to Nine Days (table 3): Ten cubic centimeters of blood withdrawn from the femoral vein was mixed with 2.5 cc. of sterile sodium citrate solution and centrifuged. The plasma was withdrawn and incubated.

No meningeal signs [24] were observed in 3 animals at the five hour interval, as shown in table 3. The spinal fluid showed only a mild cellular and protein response.

(*d*) Autogenous Blood Serum Incubated at Body Temperature for Seven to Nine Days (table 3): The blood was defibrinated and centrifuged, and the supernatant fluid, the serum, was incubated for the specified time.

TABLE 3.—*Meningeal Response Five Hours Following Intracisternal Injection of Autogenous Plasma and Serum Incubated at Body Temperature for a Specified Number of Days*

Experiment No.	Incubation, Days	Cerebrospinal Fluid: White Blood Cells, per Cu. Mm.	Cerebrospinal Fluid: Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Clinical Signs of Meningitis
53*	4	...‡	...	0	None
55*	4	240	202	1	None
83*	9	240	27	0	None
80†	10	300	368	0	None
91†	7	60	190	0	None
98†	8	...	...	0	None

* Plasma.
† Serum.
‡ Two days later, the spinal fluid contained only 1 leukocyte.

No meningeal signs or hyperthermia was present at the five hour interval in the 3 animals. The spinal fluid showed only a mild irritative response (table 3).

(*e*) Autogenous Red Blood Cells Incubated at Body Temperature for Four to Eight Days (table 4): After the plasma was removed, the red blood cells were washed three times and the supernatant wash water discarded; the packed red blood cells were incubated. After the incubation period, the specimens contained an average of 1,000,000 degenerated red blood cells per cubic millimeter and a large amount of stroma.

24. Before the entire 2 cc. of plasma had been injected into the cisterna magna of 4 dogs, opisthotonos occurred. One animal died as a result of acute respiratory failure, and the remaining 3 dogs were kept alive by means of oxygen. Within two to two and one-half hours after this reaction the animals walked, played and ate and continued so for the remainder of the day. When 2 cc. of 2.5 per cent sodium citrate was introduced intracisternally alone, opisthotonos resulted, thereby indicating that the immediate reaction was due to citrate and not plasma.

The nuchal rigidity was so pronounced that slight flexion of the neck was not possible without eliciting pain in 5 dogs, and malaise was severe in 6 of the 7 animals. The cerebrospinal fluid withdrawn at the five hour interval revealed an intense cellular reaction, varying from 2,300 to 6,000 leukocytes per cubic millimeter. The temperature

TABLE 4.—*Meningeal Response Five Hours Following Intracisternal Injection of Autogenous Red Blood Cells Incubated at Body Temperature for Four to Eight Days (Degenerated Red Blood Cells)*

Experiment No.	Incubation, Days	Cerebrospinal Fluid: White Blood Cells, per Cu. Mm.	Cerebrospinal Fluid: Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Severity of Clinical Signs of Meningitis: Malaise	Severity of Clinical Signs of Meningitis: Stiffness of Neck
52	4	.....	.....	3.4	Severe	Severe
56	4	3,650	1,170	1.8	Mild	Mild
61	4	3,200	815	2.2	Severe	Mild
71	6	4,000	...	3.0	Severe	Severe
57	7	6,000	725	2.6	Severe	Severe
72	7	2,300	550	2.2	Severe	Severe
58	8	4,000	...	1.8	Severe	Severe

TABLE 5.—*Meningeal Response Five Hours Following Intracisternal Injection of Partial Fractions of Autogenous Red Blood Cells Incubated at Body Temperature for Four Days*

Experiment No.	Fraction	Cerebrospinal Fluid: White Blood Cells, per Cu. Mm.	Cerebrospinal Fluid: Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Severity of Clinical Signs of Meningitis
107	Supernatant fluid	7,980	813	0.2	Severe
112	Supernatant fluid	5,000	718	0.0	Mild
114	Supernatant fluid	6,400	675	1.8	Moderate
113	Residue	300	508	1.4	Mild
106	Residue	400	299	2.2	None
115	Residue	560	899	1.8	Mild
110	Dialysate of supernatant fluid	10	45	0.0	None

ranged from 103.8 to 105.4 F. The spinal fluid was colorless by the fourth day, protein values normal at the end of a week and cell count normal at the end of two weeks.

(*f*) Partial Fractionation of Autogenous Red Blood Cells Incubated at Body Temperature for Four Days (table 5): (*i*) Supernatant fraction. After incubation of the red blood cells, centrifugation was carried out, but there was little separation of fluid. Most of the material remained as a red gel-like mass. To bring this mass into suspension, sufficient autogenous cerebrospinal fluid, about 2 cc., was added and the

mixture centrifuged. The chocolate-colored supernatant fluid was injected into the subarachnoid space.

Severe meningeal irritation was observed in 1 animal and a mild to moderate degree of malaise and nuchal rigidity in the other 2. However, the cellular and protein response in the spinal fluid at the five hour interval was quite marked in the 3 animals, as shown in table 5. The leukocytes ranged from 5,000 to 7,980 per cubic millimeter, and the protein values, from 675 to 813 mg. per hundred cubic centimeters. The temperatures recorded at this time ranged from 102 to 103.8 F.

(*ii*) Residue portion. Autogenous spinal fluid was added to the residue portion of the incubated red blood cells, thus forming a suspension. This fraction contained most of the stroma of the red blood cells.

Mild meningeal symptoms were observed in only 2 animals and none in the third five hours after the injection of this fraction. The cerebrospinal fluid contained from 300 to 560 white blood cells per cubic millimeter and 299 to 899 mg. of total protein per hundred cubic centimeters. The temperature ranged from 103.4 to 104.2 F.

(*iii*) Dialysate of the fluid portion. Three cubic centimeters of the supernatant portion of the incubated red blood cells prepared as described was placed in a sterile cellophane sac, securely ligated at both ends and put into a container. The sac was completely surrounded by 2 cc. of a modified Ringer solution. After eighteen hours in the refrigerator at 4 C., the dialysate was injected intracisternally.

No signs of meningeal irritation nor hyperthermia were observed in 1 dog receiving this clear colorless dialysate. At the five hour interval, the spinal fluid contained only 10 lymphocytes per cubic millimeter and 45 mg. of protein per hundred cubic centimeters.

(*g*) Hemolyzed Autogenous Red Blood Cells (table 6): A hypotonic solution was added to the red cells, causing water to enter the red cells and thereby rupturing the cell membranes and exposing the hemoglobin to the surrounding fluid.[25] The supernatant fluid contained 15 to 20 Gm. of protein per hundred cubic centimeters.

No clinical signs of meningitis were observed five hours after the injection. The cherry-colored spinal fluid showed a moderate reaction of 1,100 to 2,000 cells per cubic millimeter. A temperature above 102 F. was recorded in 3 animals. The spinal fluid was clear and colorless by the third day and free of an abnormal number of leukocytes by the tenth day.

(h) Homologous Oxyhemoglobin (table 7): The oxyhemoglobin[26] was prepared from pooled blood of 3 of the 5 dogs used in this group.

25. Hawk, P. B., and Bergeim, O.: Practical Physiological Chemistry, Philadelphia, P. Blakiston & Company, 1931, p. 378.

26. Prepared aseptically by Dr. O. Denstedt, of the department of biochemistry, McGill University.

On spectroscopic examination this solution contained only oxyhemoglobin and no other blood product.

Severe malaise and temperatures of 105 F. were noted at the five hour interval only in animals receiving relatively large amounts of oxyhemoglobin (0.135 Gm. in 5 cc.). The deeply xanthochromic cerebrospinal fluid recovered contained 4,000 to 6,000 leukocytes per cubic millimeter and 620 to 1,155 mg. of protein per hundred cubic centimeters. There was little if any stiffness of the neck.

TABLE 6.—*Meningeal Response Five Hours Following Intracisternal Injection of Autogenous Hemolyzed Red Blood Cells*

	Cerebrospinal Fluid			
Experiment No.	White Blood Cells, per Cu. Mm.	Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Clinical Signs of Meningitis
70	1,100	1,800	0.4	None
73	1,200	3,019	1.4	None
74	1,600	2,463	2.0	None
81	1,200	1,110	0.0	None
94	2,000	.....	0.0	None

TABLE 7.—*Meningeal Response Five Hours Following Intracisternal Injection of Homologous Oxyhemoglobin*

			Cerebrospinal Fluid			
Experiment No.	Solution Injected, Cc.	Oxyhemoglobin Injected, Gm.	White Blood Cells, per Cu. Mm.	Total Protein, Mg. per 100 Cc.	Temperature, Above 102 F.	Clinical Signs of Meningitis
119	0.5	0.0146	60	61	0.0	None
118	0.5	0.0146	80	81	0.0	None
117	1.0	0.027	540	187	2.0	Mild malaise
120	5.0	0.135	4,000	620	2.6	Severe malaise
121	5.0	0.135	6,200	1,155	3.6	Severe malaise

In the degenerated blood used, 0.135 Gm. of oxyhemoglobin is roughly about one quarter to one third of the total protein. Smaller amounts of oxyhemoglobin caused no meningeal symptoms and very little cellular reaction in the spinal fluid.

(*i*) Globin, a Specific Breakdown Product of Hemoglobin (table 8): A sterile modified human globin,[27] prepared from red blood cells and made up with isotonic sodium chloride solution to a strength of 0.0323 Gm. of globin per cubic centimeter, was injected intracisternally in amounts varying from 2 to 8 cc. (0.0646 to 0.2584 Gm. of globin) in an attempt to inject the amount of globin present in 2 cc. of degenerated blood.

27. Produced by Smith, Kline & French, Laboratories, Philadelphia.

No clinical signs of meningeal irritation were observed 5 hours after the injection. The cerebrospinal fluid reaction of 160 to 360 leukocytes per cubic millimeter and 384 to 812 mg. of protein per hundred cubic centimeters was commensurate with the amount of globin introduced.

(*j*) Bilirubin, a Specific Breakdown Product of Hemoglobin (table 9): These bilirubin preparations were made from bilirubin powder

TABLE 8.—*Meningeal Response Five Hours Following Intracisternal Injection of Heterogeneous Globin*

Experiment No.	Globin Injected, Cc.	Cerebrospinal Fluid: White Blood Cells, per Cu. Mm.	Cerebrospinal Fluid: Total Protein, Mg. per 100 Cc.	Clinical Signs of Meningitis
97	2	60	340	None
63	2½	180	348	None
96	4	100	532	None
64	5	380	686	None
66	8	380	812	None

TABLE 9.—*Meningeal Response Five Hours Following Intracisternal Injection of Various Bilirubin Preparations*

Experiment No.	Amount of Bilirubin Injected, Mg.	Cerebrospinal Fluid: White Blood Cells, per Cu. Mm.	Cerebrospinal Fluid: Total Protein, Mg. per 100 Cc.	Color	Temperature, Above 102 F.	Clinical Signs of Meningitis: Malaise	Clinical Signs of Meningitis: Stiffness of Neck
69	Solution A: 0.011	...	...	.....	0.0	None	None
74	Solution A: 0.022	400	237	Faint yellow	0.0	None	None
82	Solution A: 0.022	80	39	Colorless	0.0	None	None
68	Solution B: 9.684	33,000	371	Yellow	3.8	Severe	Severe
77	Solution D: 8.5*	8,000	610	Yellow	3.2	Severe	Severe
85	Solution D: 4.0*	16,000	816	Yellow	4.2	Severe	Severe
84	Solution D: 4.0*	13,760	809	Yellow	6.0	Severe	Severe
123	Solution D: 4.0*	.....	...	.....	2.0	Severe	Severe
62	Suspension 14	4,000	100	Faint yellow	0.8	Severe	Severe
65	Suspension 34	5,900	89	Colorless	2.6	Severe	Severe
111	Dialysate of D	2,000	100	Colorless	0.0	None	None

* Kept in solution at p_H 7.5 with globin.

(Eastman Kodak Co.) and put into solutions with sodium hydroxide. The p_H was neutralized with hydrochloric acid, and protein was added to the solution to insure stability and maintain a p_H of 7.5. It was difficult to keep large amounts of bilirubin in solution at a p_H of 7.5 unless a protein was present. The source of the bilirubin is immaterial, as it is a non-protein substance.

No signs of meningeal irritation were observed after injection of a weak solution of bilirubin, solution A, in experiments 69, 74 and 82. The actual amount of bilirubin introduced varied from 0.011 to 0.022

mg. The cerebrospinal fluid at the five hour interval revealed a mild reaction of 80 to 400 leukocytes per cubic millimeter and 40 to 237 mg. of protein per hundred cubic centimeters.

A very severe meningeal reaction in experiment 68 followed the injection of solution C, which contained 9.684 mg. of bilirubin. At the five hour interval the animal was semicomatose; the temperature was 105.8 F., and the yellow spinal fluid contained 33,000 leukocytes per cubic millimeter, 371 mg. of protein and 0.4 mg. of bilirubin per hundred cubic centimeters. Results of bacteriologic studies of the spinal fluid were reported as negative.

Another severe meningeal reaction followed the injection of solution D, a globin-bilirubin preparation containing 4 to 8.5 mg. of bilirubin (experiments 77, 84, 85 and 123). The temperature ranged from 104 to 108 F. The recovered yellow spinal fluid contained from 8,000 to 13,760 leukocytes per cubic millimeter, and over 1 mg. of bilirubin per hundred cubic centimeters. The fluid became colorless at the end of a week and free of an abnormal number of leukocytes by two weeks.

A pronounced meningitis was also observed five hours after the injection of 14 and 34 mg. of bilirubin suspended in fresh autogenous cerebrospinal fluid in experiments 62 and 65. The clinical reaction was less than that observed after injection of the bilirubin-globin solution. The spinal fluid contained 4,000 to 5,000 leukocytes per cubic millimeter and 89 to 100 mg. of protein per hundred cubic centimeters.

No clinical manifestations of meningitis nor of hyperthermia were observed following the injection of a dialysate of solution D, but the spinal fluid contained 2,000 leukocytes per cubic millimeter and 100 milligrams per cent of protein (experiment 111).

In an attempt to obtain autogenous bilirubin, jaundice was produced experimentally in 2 dogs, in 1 by hemolysis and in the other by ligation of the common duct.[28] Both animals were quite playful and had normal temperatures. The spinal fluid showed reactions comparable to those in the experiments with whole blood.

COMMENT

Blood and its breakdown products cause cellular and protein responses of varying degrees in the cerebrospinal fluid, as summarized in tables 10 and 11 and chart 1. But the significance of this study is the comparison of meningeal reactions, since the amounts introduced were for all intents and purposes the same in each animal. The degenerated erythrocyte contains the material responsible for the toxicity observed when blood is present in the subarachnoid space. Autogenous "fresh" whole blood, serum and plasma in comparable qauntities caused only a mild cellular response and no objective changes.

28. The animal with ligated common duct became jaundiced after three days, with a blood bilirubin value compatible with obstructive jaundice.

The five hour cellular reaction in all experiments except those with supernatant dialysate consisted of polymorphonuclear cells, while after twenty-four hours the lymphocyte was the predominant cell.

The difference in reactions obtained after the injection of whole blood or serum between this study and others may be readily attributable to several factors. Bagley [19] repeatedly introduced whole blood at short intervals, thereby maintaining a state of chronic irritation. Ayer injected

TABLE 10.—*Summary of Meningeal Responses Following Intracisternal Injection of Blood and Its Breakdown Products*

Substance	No. of Dogs	Cerebrospinal Fluid: White Blood Cells, per Cu. Mm., Range	White Blood Cells, per Cu. Mm., Average	Protein, Mg. per 100 Cc., Range	Protein, Mg. per 100 Cc., Average	Range of Temperature, Above 102 F.	Average Temperature, Above 102 F.	Severity of Clinical Signs of Meningitis
1. Autogenous fresh whole blood	10	385- 600	457.5	273-1,130	645.0	0.0-0.8	0.18	None
2. Autogenous blood incubated 37 C. for 3-12 days	8	1,800- 4,500	3,757.0	600-1,020	804.4	1.8-5.0	3.08	Severe
3. Autogenous blood incubated 37 C. for 1-2 days	4	1,880- 2,700	2,245.0	382- 574	475.4	1.4-2.0	1.75	Mild
4. Autogenous red blood cells incubated 37 C. for 4-8 days	7	2,300- 6,000	3,858.3	550-1,170	815.0	1.8-3.4	2.43	Severe
5. Supernatant from autogenous degenerated red blood cells	3	5,000- 7,980	6,460.0	675- 813	735.3	0.0-1.8	0.66	Mild, moderate, severe
6. Residue from autogenous degenerated red blood cells	3	300- 560	420.0	299- 899	568.6	1.4-2.2	1.8	1 none; 2 mild
7. Dialysate of supernatant from autogenous degenerated red blood cells	1	.....	10.0	.....	45.0	.....	0.0	None
8. Autogenous hemolysate red blood cells	5	1,100- 2,000	1,420.0	1,110-3,019	2,008.0	0.0-2.0	0.76	None
9. Autogenous plasma and serum incubated 37 C. for 4-10 days	6	60- 300	210.0	27- 368	196.8	0.0-1.0	0.16	None
10. Oxyhemoglobin								
A:0.0146 Gm.	2	60- 80	70.0	61- 81	71.0	0.0-0.0	0.0	None
B:0.027 Gm.	1	.....	540.0	.....	187.0	.....	2.0	Mild
C:0.135 Gm.	2	4,000- 6,200	5,100.0	620-1,155	843.0	2.6-3.6	3.1	Severe
11. Heterogeneous globin	5	60- 380	220.0	340- 812	543.6	0.0-0.0	0.0	None
12. Bilirubin								
A:0.011-0.022 mg.	3	80- 400	240.0	39- 237	138.0	0.0-0.0	0.0	None
B:4.8 mg. with globin.....	4	8,000-16,000	12,587.0	610- 899	775.0	2.0-6.0	3.85	Severe
C:Suspension 14-34 mg.....	2	4,000- 5,900	4,950.0	89- 100	95.0	0.8-2.6	1.7	Severe

relatively large amounts in small animals (3 cc. into rabbits weighing 2 to 3 Kg.).

The supernatant portion of the degenerated red blood cells in the subarachnoid space is so much more irritating than the residue and dialysate fractions that many substances therefore may be dismissed from consideration as being toxic in this locale.

The stroma of the red blood cell can be disregarded as a toxic agent since the residue portion contained autolysed and degraded cell debris. Some methemoglobin was probably adherent to the stroma of the degenerated red cells and not in a free state, or perhaps, not in sufficient quantity. The supernatant fraction would contain free methemoglobin, oxyhemoglobin, red blood cell enzymes, phospholipids and glycolipids, as well as many soluble substances such as salts, urea, uric acid, amino

acids, and lactic acid. The latter soluble substances are all dialysable and presumably therefore not responsible for the toxicity. Indeed, many are normally present in the spinal fluid. Even though some phospholipids and glycolipids are probably present in the supernatant portion, they would be, for the most part, associated with the residue fraction.

Oxyhemoglobin, which colors a solution dark red, appears to be responsible for some of the meningeal symptoms observed and can account for the pronounced cellular and protein response in the spinal fluid when present in sufficient amounts. It is interesting to note that stiffness of the neck was absent in these experiments though a pronounced polymorphonuclear reaction was present in the spinal fluid. Methemoglobin might also be a toxic substance, as all injected fluids causing severe meningeal reactions were chocolate-colored, which is

TABLE 11.—*Summary of Clinical Responses Following Intracisternal Injection of Blood and Its Breakdown Products*

Absence of Stiffness of Neck and Malaise	Presence of Stiffness of Neck and Malaise
Autogenous fresh whole blood	Autogenous incubated blood *
Autogenous incubated cerebrospinal fluid *	
Autogenous incubated plasma and serum *	Autogenous incubated red blood cells *
Autogenous hemolysed red blood cells	
Solid portion of autogenous incubated red blood cells *	Fluid portion of autogenous incubated red blood cells *
Dialysate of fluid portion of autogenous incubated red blood cells *	
Weak concentration of oxyhemoglobin	Strong concentration of oxyhemoglobin
Heterogeneous globin	
Weak concentration of bilirubin	Strong concentration of bilirubin

* Incubated at body temperature for specified number of days.

presumably due to the presence of this protein. Such an observation makes one wonder whether different toxic materials in blood may be responsible for different manifestations.

Therefore, the most toxic substance of the blood to the subarachnoid space is probably contained in the heme component of hemoglobin. Hemolysed red cells, which contain free hemoglobin, caused a greater cellular response than fresh whole blood but considerably less than degenerated blood or oxyhemoglobin.

If the heterogeneous globin caused only a mild cellular reaction in the spinal fluid and no clinical signs of meningeal irritation, it seems unlikely that autogenous globin would have resulted in a greater response. Heme is composed of a porphyrin (4 pyrrole groups) and iron. On hydrolysis heme yields bilirubin, which is iron free and contains 4 pyrrole groups, but the arrangement has changed so that they no longer formed the ring structure typical of a porphyrin. Thus there most probably appears only a porphyrin, iron or bilirubin, either alone or in combina-

nation with one another, to be considered responsible for causing the toxic effects of "degenerated" blood on the subarachnoid space.

Since bilirubin is a well characterized nonprotein substance, its source is immaterial. Bilirubin or biliverdin was thought likely to be one of the causative agents for the meningeal reactions observed because of the problems encountered in solubility, the difference in reactions between suspensions and solutions and the clinical and histopathologic impressions of other authors. The meningeal responses were similar to those to the "degenerated" red blood cell.

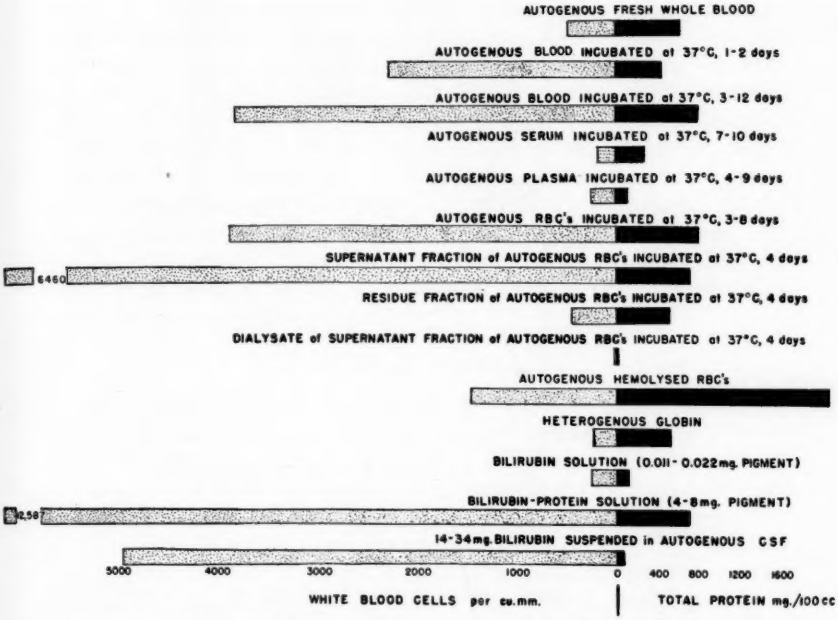

Chart 1.—Summary of the cerebrospinal fluid and protein response five hours following the intracisternal injections of the various materials used except oxyhemoglobin.

The possibility that this pigment is the causative factor in aseptic meningitis due to blood was suggested by Bagley in 1929. Spurling stated that the irritative reaction in the subarachnoid space following craniocerebral injuries is tremendously increased with the appearance of bilirubin and biliverdin formed from the disintegrated red blood cells. The difference in protein response between suspensions (88 to 100 mg. per hundred cubic centimeters) and solutions (800 to 900 mg. per hundred cubic centimeters) of bilirubin or biliverdin seems quite sig-

nificant. The latter response could not be accounted for alone by the globin, since 2 cc. of globin caused a response of only 340 mg. of protein per hundred cubic centimeters. A high concentration of bilirubin could be kept in solution at a physiologic p_H only in the presence of protein. If high concentrations of bilirubin in alkaline mediums are added to spinal fluid, considerable flocculation occurs and the xanthochromic super-

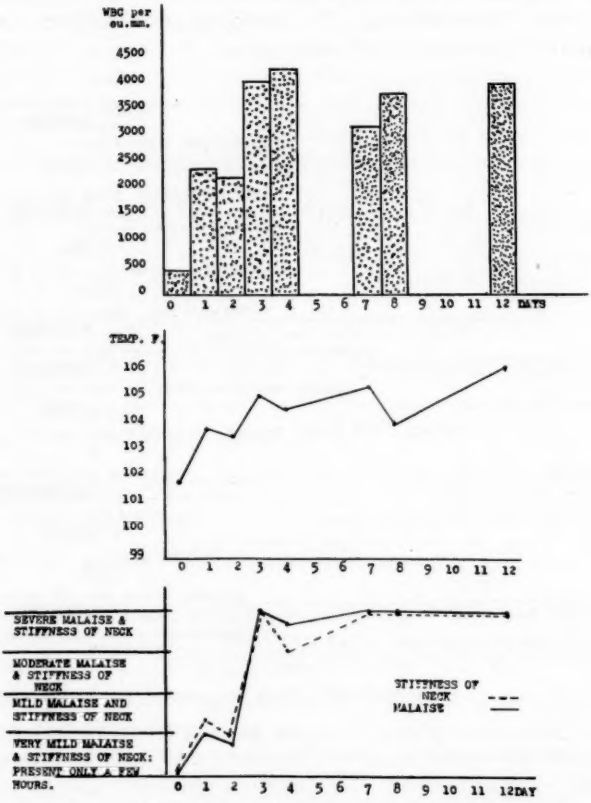

Chart 2.—Duration of incubation of autogenous blood plotted against meningeal response (pleocytosis, temperature, stiff neck and malaise) five hours after the intracisternal injection. The peak of the response occurs at three days of incubation, and then the reaction forms a plateau. Zero represents fresh blood.

natant fluid has a very low concentration of pigment. Large amounts of bilirubin in suspension have less toxic effect when injected intracisternally than do smaller amounts of bilirubin-protein solutions. Probably the subarachnoid lining is affected only by the dissolved substance and the amount of this would be low even though solid pigment is present

unless it is brought into solution by protein. It is also possible that the solid material is not readily carried from the site of injection to the rest of the subarachnoid space. These reactions suggest the possibility that when the heme is split from the hemoglobin and breaks down to bilirubin this pigment is the toxic agent. The dilution and adsorption to the protein from hemoglobin cause the bilirubin to flocculate and be absorbed by the macrophages, thereby limiting its irritative action.

The graphic portrayal (chart 2) of experimentally produced meningeal irritation by fresh blood and blood that was incubated at body temperature for one to twelve days coincides with that seen in many cases of subarachnoid hemorrhage following intracranial operation, craniocerebral injury or a leaking aneurysm. These findings are supported by Hammes, who found that when death occurred three days after rupture of an aneurysm all cells increased in number and mesothelial cells were filled with brown pigment, iron and degenerated leukocytes. This certainly indicates that at three days the irritation to the subarachnoid space had already been sustained, and it is not unlikely that after the first twenty-four hours the free degenerated blood products are the causative agents of the pronounced cellular response. Therefore, one or a combination of breakdown products of heme could well be the responsible agent, or agents, for these meningeal reactions observed after such subarachnoid hemorrhages.

CONCLUSIONS AND SUMMARY

The agent in blood causing the greatest meningeal response is present in the heme component. The specific agent probably is bilirubin or a like pigment. This has been shown in a comparative study of the reactions to blood and its breakdown products in the subarachnoid space in over 100 experiments on dogs.

The severity of the experimentally produced aseptic meningitis caused by autogenous fresh blood and degenerated blood reached a peak when the blood was three days old (chart 2). This time relationship of pronounced meningeal irritation coincides with that seen histopathologically after rupture of intracranial aneurysms and clinically in subarachnoid hemorrhage following intracranial operations, craniocerebral injuries and ruptured or leaking intracranial aneurysms.

Aseptic hemogenic meningitis is the term proposed for aseptic meningitis due to blood in the subarachnoid space, for it states the cause and differentiates this meningitis from the other aspetic meningitides.

FOCAL DISORDER OF BRAIN ACTIVITY AS IT RELATES TO THE CHARACTER OF CONVULSIVE SEIZURES

Electroencephalogram in Focal Seizures

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THE PRESUMPTION is evident that focal abnormalities of brain activity should relate to the site from which a focal seizure spreads. Much attention has been paid to the character of spread of the jacksonian seizure,[1] and the accumulated evidence has been used to theorize concerning the mode of representation of movement in the motor cortex. A study of Gowers'[2] excellent monograph emphasizes how much valuable data can be acquired when the details of jacksonian and other partial seizures are ascertained and the observations are related to knowledge of cerebral physiology. Indeed, Gowers' insight into the process of spread of seizures should excite the envy of the modern electrophysiologist, who will usually find that his recently discovered facts accord with Gowers' clinical deductions and rarely differ from them materially.

In examining the electroencephalograms of persons subject to focal convulsions, we were impressed with how frequently a single interseizure record obtained for diagnostic purposes would indicate focal abnormality in the cerebral hemisphere which presumably initiated the attack. Gibbs, Merritt and Gibbs[3] (1943) provided definite evidence for a high correlation between clinical and electroencephalographic inference concerning the site of origin of focal seizures. We became interested in establishing further correlations between the site, extent and character of brain wave disorder evident in the resting record of brain activity and the site of origin that can be imputed by clinical

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1. Walshe, F. M. R.: On the Mode of Representation of Movements in the Motor Cortex with Special Reference to Convulsions Beginning Unilaterally (Jackson), Brain **66**:104-139, 1943.

2. Gowers, W. R.: Epilepsy and Other Chronic Convulsive Diseases, New York, William Wood & Company, 1885.

3. Gibbs, E. L.; Merritt, H. H., and Gibbs, F. A.: Electroencephalographic Foci Associated with Epilepsy, Arch. Neurol. & Psychiat. **49**:793-801 (June) 1943.

investigation of the seizure pattern. The writings of Jackson and Gowers provided the working concept for classifying seizures in such a fashion that the principal correlates could be examined. Patterns of abnormality evident in the resting record only are considered in this report. Results of electroencephalography with metrazol® activation are not included.[4]

MATERIAL AND METHOD

Material.—Two hundred and nine serially collected electroencephalograms from patients with convulsive disorder were studied. The criterion of selection for the series was the existence of focal abnormality in the electroencephalogram, clinical evidence of focal origin of convulsions or both. Records obtained during and immediately after seizures were not considered, with the exception of those from 2 patients with epilepsia partialis continua affecting distal muscles unilaterally. The group showing focal abnormality associated with generalized seizures was included to provide a comparative basis for evaluating the focal seizure data. For each of several types of focal seizure the results give an estimate of the chance that a single interseizure record will provide a tracing which can be correlated with the presumed site of origin of the attack.

Seventy-nine of the records were from persons having exclusively generalized seizures. This number included 62 showing tonic and clonic phases of convulsions and 17 showing generalized nonconvulsive attacks. For all the latter there was clinical proof of the existence of a convulsive disorder. One hundred and thirty records were obtained from subjects with focal convulsions. The cases were derived from many sources; the patients' ages ranged from 6 months to 80 years. The unique significance of the study lies in the fact that the brain wave recordings were of the conventional variety performed in diagnostic laboratories during interseizure periods. Rarely were special recordings done; rarely did the opportunity of recording during a seizure present itself, and special recordings in the individual case, or serial recordings, were seldom attempted. Reliable histories were available for the vast majority of patients, and data relating to air studies were available for a minority.

Method of Recording.—The tracings were made on Grass four channel electroencephalographs at an amplification of 8 mm. per 50 microvolts or less. Routinely eight electrodes were applied to the head, four on each side, in frontal, central (vertex), occipital and midtemporal positions. Additional electrodes were attached at appropriate intermediate positions when it was evident that they would contribute significantly to a close localization of focal abnormality. A ground electrode was attached to each ear, and in monopolar recording these could be used separately or interconnected. Bipolar and monopolar records were obtained routinely. In many of the recordings an "average lead" was substituted for the conventional ear lead of the monopolar record (Bishop and O'Leary, unpublished data). A twenty-four minute record, including two minutes of hyperventilation and two minutes of post-hyperventilation, was obtained in each case.

Interpretation of Records.—Records were classified for character and spread of focal electroencephalographic abnormality. When the focal pattern was continuously evident as a difference in amplitude and frequency, it was called an amplitude

4. Kaufman, C.; Marshall, C., and Walker, A. E.: Activated Electroencephalography, Arch. Neurol. & Psychiat. **58**:533-549 (Nov.) 1947.

asymmetry. When intermittently present, it was classed as paroxysmal. The classification criteria of Gibbs, Gibbs and Lennox,[5] Jasper and Kershman[6] and Echlin[7] were considered. For our purpose we restricted interpretations of focalization in the electroencephalogram to unilateral focal abnormality, as we were concerned exclusively with how clinical and electroencephalographic data correlated in focal epilepsies. We were especially interested in fractionating the clinical phenomena of seizures; so we decided to proceed with as simple an electroencephalographic terminology as was possible. In doing so, we fully recognized the necessity for careful descriptive terminology in electroencephalographic study. We consider spike-wave and spike patterns the outstanding paroxysmal forms but have not subclassified them by frequency. Neither have we subclassified fast or slow focal abnormalities, being satisfied of focal character when any unusual pattern had a constant shape sequence and maintained a consistent origin beneath one or a group of neighboring electrodes. Records described by Gibbs, Merritt and Gibbs[3] as focal petit mal and petit mal variant types both appear in the present grouping as spike-wave focal records. Slow waves of quick rising phase and all paroxysmal slow patterns were grouped under slow wave sequences. No records presenting 3 per second nonfocal spike and dome activity appear in the series, perhaps because the manner of selection of case material tended to minimize the possibility of their occurrence. In rare instances there have been brief paroxysmal sequences of combined fast and slow activity of moderate amplitude that were repeated in the same unique form at intervals during the record. We have referred to these as wave complexes.

In stating the area over which a disordered pattern in the electroencephalogram was evident, we refer to diffuse and discrete focal abnormality. The term discrete is used when the polarity and amplitude of the potential suggest its relation to a single electrode. Diffuse foci might involve an anterior triangle, formed by frontal, vertex and temporal electrodes, or a posterior triangle, formed by the occipital, vertex and temporal electrodes. Any pattern recorded over a whole hemisphere was designated hemispheral. Steadily maintained differences in amplitude and pattern distinguishing between anterior and posterior triangles in opposite hemispheres, or the whole hemispheres, have been designated as amplitude asymmetries. Unless there were specific reasons to the contrary, we regarded the activity of the hemisphere over which high amplitude prevailed as the more disordered. An obvious exception in determining relative hemispheral abnormality occurred when a normal 11 per second frequency was evident on the high amplitude side and, by comparison, patterns over the opposite hemisphere were dysrhythmic or showed evidence of suppression. An equivocal finding occurred when the leads over one hemisphere recorded lower amplitude fast activity and those over the other hemisphere higher amplitude slow activity.

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5. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Classification of Epileptic Patients and Control Subjects, Arch. Neurol. & Psychiat. **50**:111-128 (Aug.) 1943.

6. Jasper, H. H., and Kershman, J.: Electroencephalographic Classification of the Epilepsies, Arch. Neurol. & Psychiat. **45**:903-943 (June) 1941. Jasper, H. H.: Electroencephalography, in Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941, chap. 14, pp. 380-454.

7. Echlin, F. A.: The Electroencephalogram Associated with Epilepsy, Arch. Neurol. & Psychiat. **52**:270-289 (Oct.) 1944.

The clinical classification of focal seizures suited the available material. Many cases fitted clearly into one or another group. However, the desire to classify accurately by the initial phenomena of a seizure became difficult when such a complication as "colored lights" in one visual field was immediately succeeded by an adversive phenomenon such as turning of the head and eyes. Thus, occasionally the clinical character of a seizure might allow it to be fitted into several groups. We have classified cases presenting evidence of both partial and generalized seizures with the partial variety because of the localizing value of the initial events. When partial phenomena occurred which were individually classifiable, such as olfactory aura succeeded by jacksonian march, the seizure was grouped under the initiating component, even though the subsequent occurrence was the more objective one. The classification follows:

1. Generalized convulsive seizures: abrupt onset; sudden loss of consciousness; falling; tonic and clonic convulsions.

2. Generalized nonconvulsive seizures: abrupt onset; sudden loss of consciousness; falling; convulsive movements not apparent. Such seizures may be confused with syncopal attacks.

3. Hemiseizures: nearly simultaneous involvement of unilateral musculature. At least a majority of the seizures show spasm restricted to the same side; rare seizures have been unilateral with no constancy as to the side affected (also noted by Gowers).

4. Partial seizures: all seizures which proceed slowly enough that the subject can analyze his feelings or note the progress of spasms before losing consciousness. Loss of consciousness may not occur or may be incomplete.

a. Partial jacksonian[8]: spasm commencing in a hand, a foot or a side of the face. Numbness in the initiating part may precede the spasm.

b. Partial, adversive: lateral deviation of the head and eyes initiating the seizure (the more general phenomenon of twisting of the whole body in the same direction occurred in 2 cases). Investigations of the physiology of the human cortex suggest the existence of several adversive fields in each of which electrical stimulation produces movement of head and eyes away from the hemisphere being stimulated. The best known of these, Brodmann area 6aB, is situated on the posterior part of the superior frontal gyrus. Similar component movements may be seen with electrical stimulation of area 5 in the superior parietal lobule and of area 22, the temporal extrapyramidal area.[9]

c. Partial, others: partial seizures not classifiable under one or another of the previously designated divisions, forming a small and diverse group. In this group are included "blank spells" in which the clinical data did not support the existence of petit mal epilepsy, spells commencing with visual, vertiginous or olfactory aura and "psychic" seizures of varied character but fleeting duration.

Figure 1, a histogram, indicates the relative proportions of generalized convulsive and nonconvulsive seizures, hemiseizures and jacksonian, adversive and other partial seizures. The total number of patients in each group was divided arbitrarily into three age ranges using the fourth and tenth birthdays as the points

8. Jackson, J. H.: Convulsive Seizures (Lumleian Lectures), Lancet **1**:685, 735 and 785, 1890. Mercier, C.: The Phenomena of Convulsion, Brain **4**:325-338, 1881-1882.

9. Foerster, O.: The Motor Cortex in Man in the Light of Hughlings Jackson's Doctrines, Brain **59**:135-159, 1936.

of cleavage. The age separation was made to provide comparisons between focal abnormalities associated with generalized and focal seizures at different ages.

In relating distributions of abnormality the term hemisphere is used without designating the side. Localized abnormality over the hemisphere ipsilateral to the spasm was very rare, and unless specifically indicated otherwise the contralateral hemisphere gave the focal pattern.

RESULTS

Examples illustrating the character of focal electrical disturbances recorded are presented in figures 2 (children) and 3 (adults). Corresponding left-sided and right-sided combinations are illustrated in each case, one or the other having the focal abnormality. Obviously the focal patterns in generalized seizures do not present the opportunity

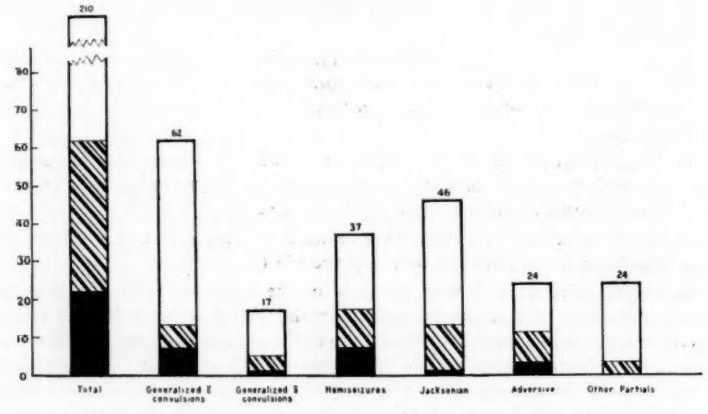

Fig. 1.—A histogram in which the relative heights of the separate columns indicate the proportion of cases that fell within each class of convulsions as compared with the total of 210 cases. The columns are divided chronologically. Each base indicates the proportion of cases recorded before the fourth birthday, each intermediate portion the cases between the fourth and the tenth birthday and each top the remainder.

for topical correlation with clinical impression. Figure 4 gives the numerical distribution of different characters of focal abnormality over the parts of the hemisphere. Each convulsive class is presented separately.

1. *Generalized Seizures with Convulsions.*—The 62 cases of generalized convulsive seizures with focal abnormality are controls collected serially with the records of focal epilepsies. They represent the total number of such cases, but more adequate history taking might have resulted in some of these being reclassed as cases of focal seizure. The over-all age distribution of the group was 6 months to 80 years. In 23 of the 62 cases (37 per cent) there was a traumatic, a meningitic

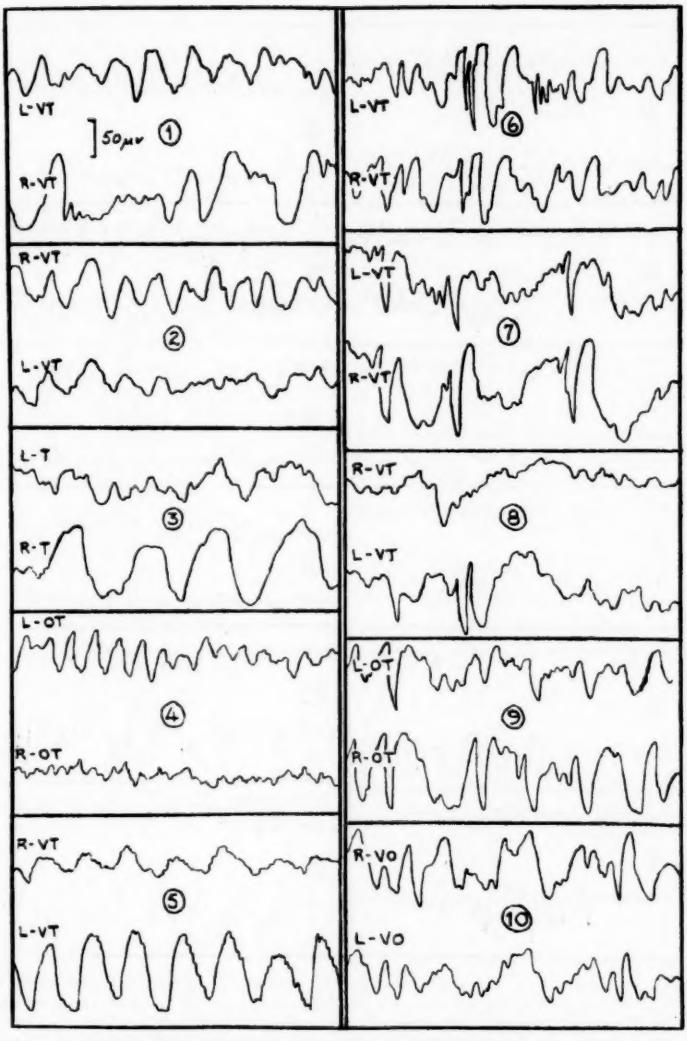

Fig. 2.—Characters of focal abnormality evident in children. For each case corresponding left and right bipolar combinations are illustrated to demonstrate the differences in activity over the two hemispheres, and the high amplitude member of each pair of records is considered abnormal. The records in the left column show continuously evident abnormality; records in the right column, paroxysmally recurring patterns. (*1*) Age 6 months; generalized seizure. (*2*) Age 10 months; birth injury; left hemiparesis; generalized convulsions. (*3*) Age 4 years; alternating adversive seizures; initiating component head and eyes to right; subsequently head and eyes to left. (*4*) Age 6 years; blank expression with subsequent limpness right arm and leg, one minute's duration. (*5*) Age 8 years; right hemiseizures. (*6*) Age 6 months; right adversive seizures, extension of right leg. (*7*) Age 6 years; left adversive seizures, spasm principally confined to left side. (*8*) Age 9 years; twitch of right side of face and aphasic component. (*9*) Age 9 years; left adversive seizures. (*10*) Age 4 years; right hemiseizures; records inconsistent with clinical data. *L* indicates left; *R*, right; *VT*, vertex-temporal; *OT*, occipitotemporal; *VO*, vertex-occipital; *T*, temporal, monopolar.

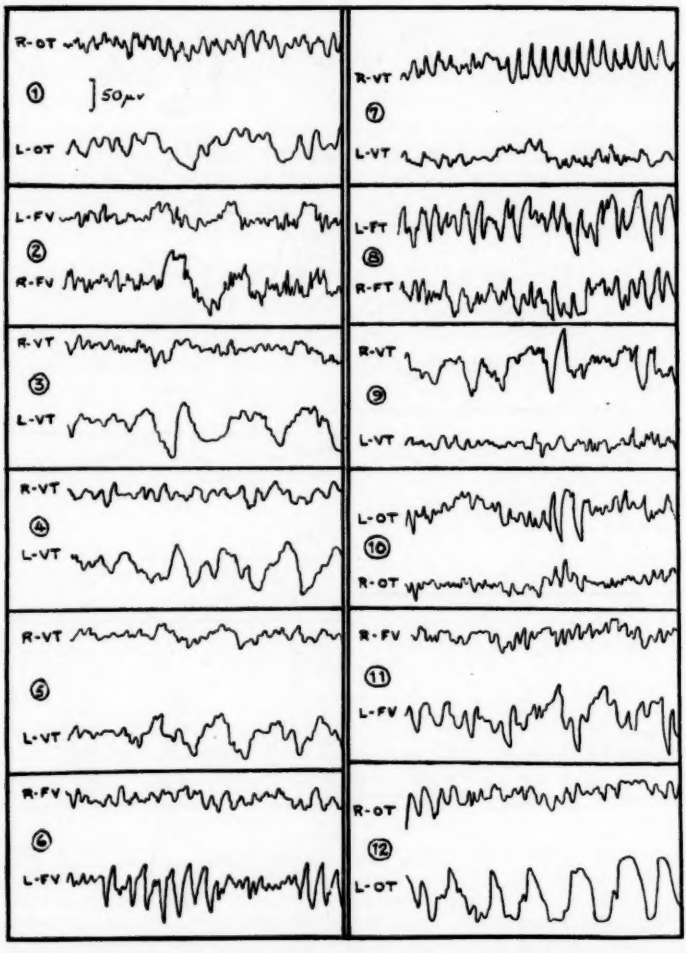

Fig. 3.—Characters of focal abnormality evident in convulsive disorders in adults. The records in the left column illustrate continuously evident abnormality; those in the right column, paroxysmally recurring patterns. (*1*) Age 33 years; right hemiseizure with interseizure quivering of right side; left slow wave focus. (*2*) Age 31 years; generalized seizures since infancy; recently changed to left jacksonian (hand signal); slow wave focus in right anterior triangle; astrocytoma of right frontal lobe. (*3*) Age 26 years; post-traumatic, right adversive seizures; quivering of right fifth digit. (*4*) Age 35 years; post-traumatic right hemiseizures; left hemispheral slow wave pattern. (*5*) Age 33 years; right hemiseizures; hemispheral amplitude asymmetry; higher amplitude and slower on left. (*6*) Age 38 years; postoperative course following removal of a parasagittal meningioma; recurrence of right adversive seizures. (*7*) Age 31 years; fleeting partial seizures; 8 per second paroxysmal slow pattern discretely localized to the left temporal electrode. (*8*) Age 44 years; jacksonian (right hand signal) spike pattern from left vertex. (*9*) Age 44 years; psychic seizures; temporal electrode; discrete pattern, slow spike. (*10*) Age 32 years; generalized nonconvulsive seizures; focal spike wave from left region. (*11*) Age 63 years; right hemiseizure; left anterior slow wave focus. (*12*) Age 15 years; partial seizure, aura of blindness; left posterior slow wave focus. *L* indicates left; *R*, right; *VT*, vertex-temporal; *OT*, occipitotemporal; *FV*, frontal-vertex; *FT*, frontotemporal.

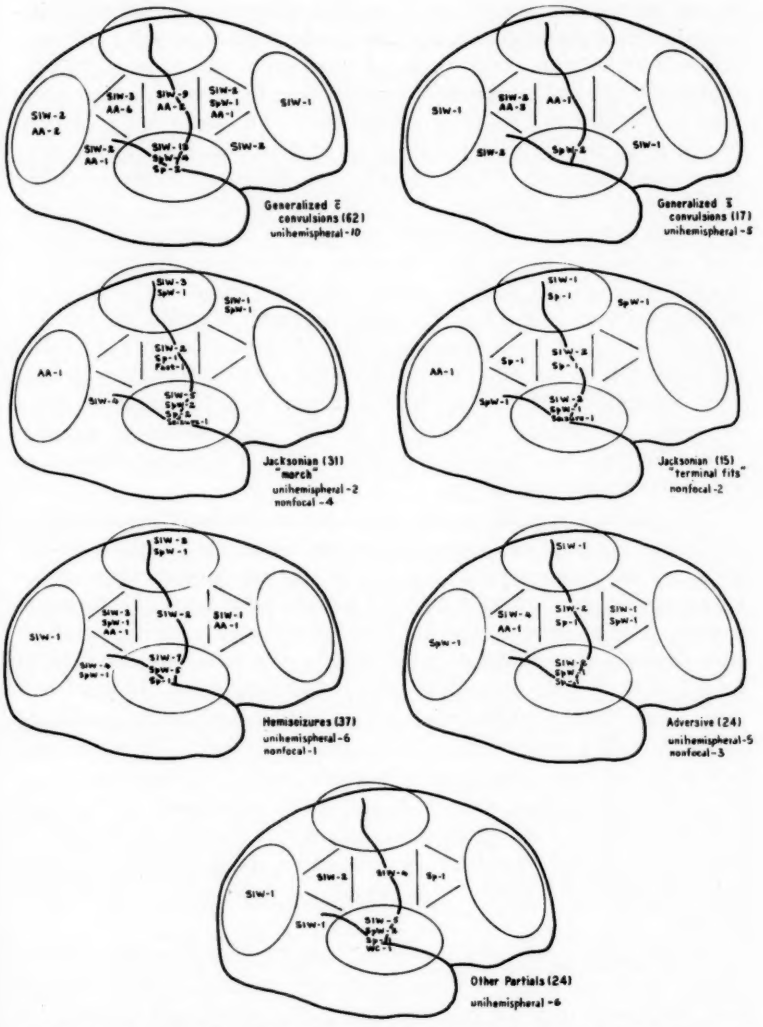

Fig. 4.—Lateral views of the cerebral hemisphere with circumscribed ovals to schematize the relations of discrete and diffuse foci. Frontal, vertex, temporal and occipital positions are indicated. Discrete focal patterns related principally to one electrode are entered within the ovals; diffuse focal patterns outside the ovals relate to the part of the hemisphere over which the disturbance in pattern was recorded. Nonfocal and hemispheric focal patterns are noted beside their respective figures. Total numbers indicate the frequency of occurrence of each abnormality with relation to its sites of occurrence. *SlW* indicates slow wave focus; *SpW*, spike-wave; *WC*, wave complex; *Seizure*, recorded during seizure; *AA*, amplitude asymmetry.

or an encephalitic history or a verified diagnosis of diffuse hydrocephalus, cerebral neoplasm, cerebrovascular disease, syphilis, tuberous sclerosis or subdural hematoma. A number of the patients (20 per cent of the 62) had hemiparesis, hemiplegia or localized unilateral weakness attributable to a lesion of the forebrain. In only 3 of the 11 cases of this series in which the results of air studies were known to us were these results negative. Of the other 8 cases, there were 3 cases of diffuse hydrocephalus (in children), 1 of diffuse cortical atrophy subsequent to trauma to the head, 2 of cerebral neoplasms, 1 of tuberous sclerosis and 1 of subdural hematoma. In comparison with routine electroencephalographic tracings on patients presenting generalized convulsions but without evidence of focal electroencephalographic abnormality, the percentage of organic involvement was high. Gibbs, Merritt and Gibbs [8] estimated that 58 per cent of a group of 160 epileptic patients with focal electroencephalographic abnormality had neurologic localizing symptoms or signs. In contrast, they stated that clinical evidence of localized damage to the brain was present in only 1 per cent of patients without an electroencephalographic focus.

To provide comparative data on a chronologic basis, we arbitrarily divide the material into three age ranges, using the fourth and tenth birthdays as dividing points. Seven of the 62 patients were in the lowest age range. Among their records were 3 diffuse amplitude asymmetries, 3 spike-wave foci and 1 hemispheral slow pattern. Another slow sequence was focalized to the vicinity of a temporal electrode, as were 2 of the 3 spike-wave focal records just mentioned. In the 4 to 9 year group there were 6 patients, 4 of whom had diffuse amplitude asymmetries, 1 a slow wave and 1 a spike-wave focus. The 47 patients in the highest age range showed a predominance of slow wave foci. There were 35 of these, variable in amplitude, in frequency (1 to 8 per second), in area of distribution, and in per cent time of appearance of slow activity during recording. In comparison, there were but 10 amplitude asymmetries (usually hemispheral), 2 spike-wave and 1 spike pattern.

Of the entire group of 62 patients, only 10 showed complete hemispheral involvement. Of the remainder, the majority of focal patterns were distributed over the posterior half of the hemisphere. Only 7 of the whole number of focal patterns appeared to involve principally the anterior triangle combinations, as compared with 29 having their principal disorganization in the central area, and 16 having the distribution of abnormality over the posterior scalp region.

Throughout the group there was no significant tendency for one or another character of focal pattern to be related to a particular area or to be discretely focalized rather than diffused although amplitude asym-

metries were usually more diffuse in their distribution than focal patterns. Significantly more of the discrete focal patterns were recorded over the posterior half of the hemisphere.

2. *Generalized Nonconvulsive Seizures.*—The 17 cases so classified were segregated from the cases of generalized convulsive seizures to test whether or not those having less severe clinical manifestations showed any differences in distribution or degree of abnormality. For other purposes these cases belong with the generalized seizure control group already discussed. The over-all age distribution was 20 months to 68 years. Because of the small number of cases the group was not divided chronologically. However, figure 1 shows the proportion of patients in each of the three age ranges. Evidence of neurologic abnormality was infrequent, only 1 of the 17 patients presenting focal neurologic signs. The topical distribution of abnormal patterns was like that of the group with generalized convulsive seizures; there was no significant difference between the two classes in the character of focal patterns, and there was the same tendency for discrete patterns to focalize over the posterior half of the hemisphere. However, proportionately, the abnormal patterns tended to be more diffusely distributed: 1 amplitude asymmetry, 2 spike-wave, 1 spike and 1 slow wave pattern had hemispheral distribution. There were also 4 less diffuse amplitude asymmetries. Two spike-wave patterns were related to temporal electrodes. Relatively discrete slow wave focal patterns were distributed as follows: occipital 1, posterior triangle 2, occipitotemporal 2 and frontotemporal 1.

3. *Hemiseizures.*—Thirty-seven persons had seizures in which the spasm was confined to one side of the body in all or in a significant number of attacks. Those few patients in whom the spasm was initiated simultaneously in an entire arm were classified with the hemiseizure group; again it happened occasionally that the character of attack changed and an initially generalized seizure was reduced to a hemiseizure.

Hemiseizures belong to the class of "unilateral involvement" in which Jackson and Gowers have emphasized a high incidence of cerebral lesions. Thus it might be expected that the hemisphere contralateral to the spasm would present electroencephalographic evidence of abnormality overshadowing that of the ipsilateral hemisphere. For instance, if patterns recorded over the two hemispheres were distinguished by amplitude asymmetry, that of the suspected hemisphere should present the greater abnormality.

The over-all age distribution was 18 months to 59 years. In 10 of the 37 cases (27 per cent) a neurologic diagnosis was established on a traumatic, meningitic, neoplastic or cerebrovascular basis. In 38 per cent of the total cases there was hemiparesis, hemiplegia or local uni-

lateral weakness attributable to a lesion of the forebrain. There was a partial overlap between these two perspectives of neurologic involvement, and the total figure for organic origin was 51 per cent. There were 3 cases in which pneumoencephalograms showed no abnormality, and in 2 of these focal neurologic signs were evident.

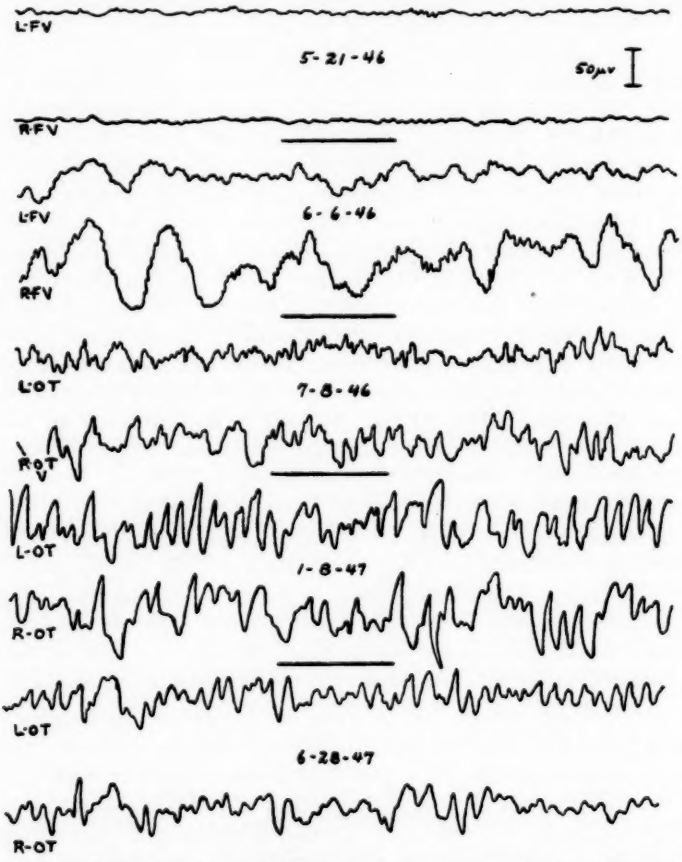

Fig. 5.—Serial recordings illustrating the changes in brain activity which occurred in a single case of left unilateral seizure with established cause (influenzal meningitis). A single unilateral spasm that occurred during an attack of influenzal meningitis set the pattern for a series of daily unilateral seizures that occurred seven months later. The initial record taken during the acute phase (May 21, 1946) showed complete suppression of activity in all leads. Thereafter, as convalescence occurred, all records showed higher amplitude over the right hemisphere. Spike and spike-wave processes appeared relatively late in the record from the right hemisphere, being recorded several weeks after a series of daily left hemiseizures. The final record, obtained thirteen months after the first, was taken at a time when seizures were under control. The spike-wave pattern continued to be recorded from the right hemisphere leads.

In the youngest chronologic group there were 7 cases: 1 nonfocal slow pattern, 1 hemispheral amplitude asymmetry and 5 discrete focal abnormalities. Two of the latter were of slow wave and 3 of spike-wave character. There were 10 cases in the 4 to 9 year group: 3 were hemispheral amplitude asymmetries; 3, spike-waves; 1, a spike, and 1, a slow wave pattern. In the range over 9 years there were 3 with amplitude asymmetries (1 hemispheral; 2 less diffuse), 2 with spike-waves and 15 with slow wave foci. The preponderance of slow wave foci among adults, also noted in the group with generalized convulsive seizures, was evident.

The focal abnormalities in this group had the same pattern distribution as that observed for the group with generalized convulsions; however, there was an even greater tendency for the focal abnormalities to be concentrated over the posterior half of the hemisphere. The outstanding feature of the group was the consistency with which focal abnormality was related to the suspected hemisphere. The only exceptions were 1 case in which the abnormality was nonfocal, 2 cases with amplitude asymmetries having low amplitude on the side of the suspected hemisphere (equivocal results) and 1 case in which the ipsilateral hemisphere presented the focal pattern.

4. *Jacksonian Seizures.*—In deciding which seizure patterns to classify as jacksonian we were guided by Jackson's publication in *The Lancet,* 1890.[8] There Jackson wrote of four degrees of progress in this seizure manifestation: (1) terminal, the seizure remaining in the distal part; (2) monospasm, with march involving a single extremity; (3) hemispasm, proceeding on to involve one entire side of the body, and (4) bilateral, resulting in generalized involvement. For our purpose it was convenient to separate jacksonian seizures into two categories: those in which the fit remained terminal, and those in which march occurred. We have also adopted Jackson's term signal symptom to indicate the point at which a march commenced.

Thus classified, in 15 of our cases the seizure commenced in one or more terminal parts and did not spread and 31 showed march. The total number of cases studied was 46. Of the 15 terminal fits, 4 occurred in the face, 4 in the hand, 2 in the hand and foot and 1 in face, hand and foot. Of the 31 seizures with march, 10 commenced in the face, 14 in the hand and 6 in the foot (also 1 seizure record). It will be noted that terminal seizures may well involve two or even three signal symptoms (as face, hand and foot), whereas in march cases the seizures spread from one signal symptom. The over-all age distribution in the entire jacksonian class was 3 to 66 years. In 10 of the 46 cases (22 per cent) a neurologic diagnosis was established on a neoplastic, post-traumatic, meningoencephalitic, syphilitic or cerebrovascular basis. In 26 per cent of the total cases there was neurologic evidence of hemiparesis, hemiplegia or circumscribed weakness of a terminal

part. Since partial overlap between the two perspectives of neurologic involvement occurred, the total figure established for organic origin was 43 per cent. However, it is important that when seizures were confined to the terminal part, only 1 of 15 cases could be designated as having objective evidence of neurologic involvement. When such cases of terminal seizure were subtracted from the total, the incidence of neurologic impairment in jacksonian march seizures rose to 61 per cent. In 10 of the 46 cases results of air studies were negative; in 5 other cases there were evidences of abnormality; data were not available for the entire series.

Of the 15 seizure patterns of terminal character, there was 1 normal record and 1 nonfocal definitely fast dysrhythmia. The remaining records were focal, and the abnormalities were evident over the hemisphere contralateral to the signal symptom. Of these, there were 3 spike, 3 spike-wave and 5 slow wave foci. In addition there was 1 repetitive spike focal seizure pattern. The incidence of focal abnormality was significantly higher in the central area, there being but 1 focus situated anterior to the central area and 2 posterior to it. The attempt was also made to relate the epicenter of brain wave disturbance to clinical deduction from the terminal site affected. In terminal seizures there appeared to be no significant relation between greater abnormality at the vertex electrode in the case of "foot" signals and at the temporal electrode in the case of "face" signals. It was our impression (impossible to substantiate in figures) that the foci were relatively less discrete in the terminal seizures than in the march seizures.

Four of the 31 cases of march seizures had nonfocal records, and 1 other record was an indefinite occipital amplitude asymmetry. All other records were focal, the significant abnormality being apparent over the contralateral hemisphere. Two were hemispheral focal patterns belonging to the amplitude asymmetry type. There were 15 slow wave, 4 spike-wave and 3 spike foci. Again the majority of abnormal patterns were clustered in the central area; but 4 slow foci were recorded over the posterior temporal area, and there were 2 other foci situated anterior to the central area. Examined from the viewpoint of relation between epicenter of disturbance arrived at by clinical deduction and on electroencephalographic basis, there again appeared to be no consistent relation between "foot" signals and vertex, "face" signals and the temporal electrode, although the "face" signals did appear in largest numbers in relation to abnormality recorded principally at the temporal electrode. Two cases in which the wasting of the hand pointed to longstanding cortical lesions (ages 36 and 42) showed no more discrete foci than some of those in which evidence of neurologic involvement was absent.

In both terminal and march categories amplitude asymmetries were significantly less common than in the generalized seizure and hemi-

seizure groups. Other focal characters had approximately the same proportion. Also, as compared with the latter groups, we believe the seizure patterns to have been relatively more discrete and more clustered over the central area of the hemisphere.

5. *Adversive Seizures.*[10]—These commence with turning of the head and eyes toward the side opposite to the suspected hemisphere or torsion of the entire body in that direction. After such preliminary spasm, the seizure may become generalized. Twenty-four cases were so classified, 1 of which belonged to the alternating type.

The over-all age distribution in the 24 cases was 6 months to 52 years. In 7 of the 24 cases (30 per cent) a neurologic diagnosis was established on a traumatic, neoplastic or hydrocephalic basis. In addition, there was 1 case of tuberous sclerosis and a chronic viral encephalitis. There were 3 additional cases of undertermined cause with focal neurologic signs; hence 46 per cent of the entire group showed clinically definite evidence of neurologic involvement.

The youngest age group contained 1 hemispheral amplitude asymmetry, 1 nonfocal spike-wave pattern and 1 hemispheral slow wave focus. In the 4 to 9 year group there were 2 focal and 1 nonfocal spike-wave records and 6 slow wave foci, 2 of which were hemispheral, 3 confined to the posterior triangle and 1 discrete and related principally to a temporal electrode. In 12 cases in the oldest chronologic group, 2 records were amplitude asymmetries, 1 was a spike-wave pattern focal to the anterior triangle and 2 were spike patterns with foci in the central area. There were also 7 slow patterns. One of the latter was nonfocal, 1 involved an anterior and 1 a posterior triangle; 4 were concentrated in the temporal area. The tendency observed in the generalized and hemiseizure groups toward a numerical increase in slow wave foci in the older age range was not definite here. With 1 possible exception, the alternating adversive seizure mentioned, all focal patterns appeared over the hemisphere away from which the head and eyes turned at the start of the seizure.

6. *Partial Seizures, Other.*—A miscellany of 24 cases are grouped under this heading. These included brief seizures distinguished by visual, vertiginous, auditory or olfactory aura, psychic seizures and "blank spells." Several cases in this group resembled the "partial seizures" with visual disturbance originally described by Jackson (1863).[11] Psychic seizures included fleeting experiences of unreality

10. Two cases of adversive seizures (recent origin) recorded after the series was closed showed anterior triangle foci and were of neoplastic origin. In 1 the pattern was of spike-wave and in the other of slow wave character.

11. Jackson, J. H.: Unilateral Epileptiform Seizures Attended by Defect of Sight, Epileptiform Seizures: Aura from Thumb; Attacks of Colored Vision, M. Times & Gaz. **1**:588-589, 1863.

(sometimes brief feelings of terror or of impending calamity) and very brief psychomotor processes in which the subject stared, walked a few steps automatically and exhibited manifestations of rage. Five "blank spells" were also included in the group because there was an established history of antecedent trauma, meningitis or encephalitis and the record of brain activity exhibited focal abnormality. In none of the cases was there 3 per second spike and dome activity; true psychomotor seizures were eliminated.

The age distribution of the group was from 5 to 75 years. Evidence of organic involvement was minimal. In 1 case the patient had hemiplegia and uncinate fits; a small calcified tumor was removed. In another the air studies presented evidence of ventricular dilatation, and in a third there was mild change in one occipital horn (partial, visual aura, unilateral occipital slow spike).

Partial seizures characterized by special aura included 3 visual, 2 auditory, 2 uncinate and 1 aphasic seizure. Some of the patients also had generalized convulsive seizures. In 2 of the 3 cases with visual aura there were unilateral occipital foci. In the 2 cases with auditory aura and the 1 with aphasic aura there was abnormality from the temporal area. Of the 2 cases with uncinate attacks, there was hemispheral slow activity in 1 and in the other an inferior temporal paroxysmal slow pattern. In the latter cases the uncinate attacks frequently were followed by jacksonian march seizures, the signal movement for the latter being in the hand. The paroxysmal slow sequences were recorded over the temporal area contralateral to the signal movement. The 2 psychic seizures observed had temporal focal abnormality, 1 represented by a unique complex of fast waves and the other by a slow wave focus. The 5 blank spells studied presented a variety of patterns, including amplitude asymmetry, slow wave, spike and spike-wave forms.

The only noteworthy tendency in the group (excepting in cases with visual aura) was for discrete foci to cluster about the temporal electrode.

COMMENT

Only brief mention is made of the excellent studies by Jasper and Hawke,[12] and Gibbs, Lennox and Gibbs [13] on the subject of disordered electroencephalographic pattern evident during epileptic attacks. Casa-

12. Jasper, H. H., and Hawke, W. A.: Electroencephalography: IV. Localization of Seizure Waves in Epilepsy, Arch. Neurol. & Psychiat. **39**:885-901 (May) 1938.

13. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: The Electroencephalogram in Localization of Epileptic Seizures, Arch. Neurol. & Psychiat. **36**:1225-1235 (Dec.) 1936.

major, Smith, Constable and Walter [14] studied the interval records in 17 children with focal seizures. Echlin [7] studied a group of adult patients subject to convulsions that included patients presenting focal epileptic patterns. Our more general observations are not significantly different from those of these earlier related studies. Gibbs, Merritt and Gibbs [3] classified a very large group of epileptic patients that contained 160 with focal electroencephalographic abnormality. The proportion between children and adults was like that of our study, and our total series would appear almost comparable to theirs, except for our exclusion of patients with definite psychomotor disturbances and our inclusion of those with neoplastic lesions. Our over-all statistical results agree closely with those of Gibbs, Merritt and Gibbs,[3] despite some differences in selection, in the manner of recording and in classifying seizures and handling data. The close correspondence proved very satisfactory to us as an added demonstration of the effectiveness of electroencephalography as a diagnostic procedure in the focal epilepsies.

In a high percentage of the cases of focal epilepsy in this series a single electroencephalogram taken during an interseizure period revealed evidence of focal disorder of brain activity (90.7 per cent of hemiseizures, jacksonian seizures and adversive seizures, as compared with 87 per cent indicated by Gibbs, Merritt and Gibbs [3] and 77 per cent of focal cortical seizures reported by Jasper and Kershman [6]). Large numbers of electrodes applied to the scalp were not necessary to detect focalized abnormality. We believe, however, that additional electrodes are frequently necessary to localize a detected abnormality closely.

In the group with generalized convulsions (with focal disorder of pattern), with hemiseizures, with jacksonian march and with adversive seizures there was a high incidence of other neurologic involvement attributable to lesions of the forebrain. This observation also confirms prior findings by Gibbs, Merritt and Gibbs [3] and Jasper and Hawke.[12]

These other indications of neurologic disorder were evident in 61 per cent of cases of jacksonian march as compared with 51 per cent of cases of hemiseizure, 46 per cent of cases of adversive attacks and 37 per cent of control cases with generalized convulsions. By contrast, control cases without generalized convulsions (with focal disorder of pattern), cases of jacksonian terminal spasm and other cases of partial seizures presented a low incidence of other neurologic findings. Character or distribution of focal pattern did not aid in distinguishing between the classes with high and with low incidence of organic lesions.

No unique relation was discovered between the character of focal disorder and the type of seizure, cases of psychomotor disturbances and

14. Casamajor, L.; Smith, J. R.; Constable K., and Walter, C. W. P.: The Electroencephalogram of Children with Focal Convulsive Seizures, Arch. Neurol. & Psychiat. **45**:834-847 (May) 1941.

petit mal epilepsy excluded. Nor was there a significant correlation between the character of the abnormality and the region of the hemisphere over which it might be recorded. If there are differences in discreteness and character of focal disorder that distinguish focal cortical from focal subcortical lesions, these were not prominent in our study. In comparison of cases of hemiseizure and jacksonian march, there was no significant difference in distributions of pattern except for a trend toward central clustering in cases of jacksonian march. For 3 groups (with generalized convulsions, hemiseizures and jacksonian seizures) there was a significant increase in the proportion of slow foci recorded in the higher age range (over 9 years) as compared with the lower age range (younger than 10 years).

The pattern of focal abnormality evident in the resting record was almost invariably recorded over the hemisphere suspected of involvement on neurologic grounds (Gibbs, Merritt and Gibbs [8]). A small number of nonfocal, equivocal or (rarely) inconsistent results were obtained. In a significant number of cases the focal abnormality was detected over the part of the hemisphere in which clinical study would suggest a "discharging lesion." Inconsistencies in individual cases occurred when clinical data indicated a discrete lesion (as in cases of jacksonian march), whereas the topical distribution of abnormal pattern covered a much larger area. They also occurred when a relatively discrete electroencephalographic focus did not appear to relate to the site of a lesion as imputed clinically.

The relationship between character of focal pattern and the probable nature of the underlying pathologic process has important clinical significance. The opinion is held that a focal distribution of 1 per second slow waves is commonly related to an underlying neoplasm. We have confirmed this opinion repeatedly in cases of focal epilepsy and in cases with other presenting symptoms. On the other hand, we have observed cases in which vascular and neoplastic lesions had been ruled out and which showed persisting slow patterns of similar topical distribution at successive recordings. When such constantly appearing slow patterns cannot be associated with abnormality evident in air studies, we recommend serial electroencephalograms to detect extension or change in the character of the focally abnormal sequences. It is our belief that no type of focal electroencephalographic record invariably rules out the existence of an underlying neoplasm. When the presenting symptoms have existed for a prolonged period or there is other plausible cause, one may be convinced that a neoplastic source for the focal pattern is improbable. With scalp recordings over verified neoplasms we have observed focal atypical slow paroxysmal patterns, spike-wave patterns and irregularly fast patterns. Not infrequently the same

patterns may also appear in a case of focal epilepsy in which all other procedures, including air study, have given negative results. It is when the focal epileptic seizure that may be the presenting sign occurs early in the development of a subcortical tumor that atypical slow (or fast) sequences of focal character may be detected and passed over as not indicating a neoplasm. It is important to reflect that as a subcortical tumor develops, the activity of the neighboring part of the brain may undergo a series of changes before the area is so altered by tumor growth that the 1 per second slow wave becomes the prevailing focal pattern.

When there is a reliable history indicative of encephalitic or meningitic origin for focal seizures, considerable variability has been found in the character of related electroencephalographic abnormality. Slow wave and spike-wave patterns predominated, however, and a number of cases of focal seizures in our series confirm the recent study of Gibbs and Gibbs [15] indicating that focal patterns may relate to convulsions on a postencephalitic basis. We have been unable to distinguish between cases of focal seizures with encephalitic and meningitic origin by the character or extent of abnormality evident. A single case of influenzal meningitis with serial recording is reported in detail to illustrate that considerable variability may occur in the focal pattern and that spike-wave processes may appear as a relatively late electroencephalographic residual. Despite the variability noted, difference in amplitude of potential between records from left-sided and right-sided leads persisted through a thirteen month postmeningitic interval.

REPORT OF A CASE

G. C., a 5 year old white boy without family or personal history of convulsive disorder, was admitted to St. Louis City Hospital on April 30, 1946, with nausea, vomiting, incontinence and stiff neck. His illness commenced with a shaking chill followed by fever and vomiting. He had recovered from measles one week previously. Lumbar puncture on admission yielded fluid containing 7,800 white blood cells per cubic millimeter, and Hemophilus influenzae type B was isolated. The patient alternated between a restless semicomatose state and inactive stupor. On May 7 he had a hemiseizure on the left, with residual left hemiparesis. An electroencephalogram on May 21 showed almost complete suppression of activity in all combinations of leads. There were no more seizures; recovery from the acute manifestations occurred, and the hemiparesis improved. Another tracing was made on June 6. It showed a right hemispheral slow wave focal pattern, the activity of the left hemisphere being of low voltage character. A recording on July 8 gave an approximately normal frequency pattern over the left hemisphere; all combinations of leads on the right side continued to show moderate amplitude slow waves. On October 4 he commenced to have intermittent jerking in his left

15. Gibbs, F. A., and Gibbs, E. L.: The Electroencephalogram in Encephalitis, Arch. Neurol. & Psychiat. **58**:184-192 (Aug.) 1947.

arm, and in December 1946 he had daily left hemiseizures, each followed by drowsiness. Another electroencephalogram (Jan. 8, 1947) gave evidence of a 9 per second basic resting frequency over both hemispheres, but the right posterior combinations were of lower amplitude comparatively than the corresponding left-sided leads and also showed admixed slow activity. Isolated spikes and atypical spike waves appeared for the first time and were of high amplitude in the right temporal and occipital leads. In the final record of the series (June 27, 1947) activity over the right hemisphere was lower than over the left and there was a slow wave focus at the right temporal electrode. The record again showed intermittent bursts of spikes which were higher in amplitude in the right posterior lead combinations. After the daily hemiseizures of December 1946, the condition was controlled with anticonvulsant medication.

A hemiseizure pattern was first evident during the acute illness. In the ensuing months the pattern of the electroencephalogram changed continually, spike and spike-wave patterns not becoming evident until eight months following the onset of the illness. A month prior to the recording in which definitely paroxysmal sequences were detected in the record, the child had an almost daily series of hemiseizures.

SUMMARY

1. There is a close agreement between the clinical interpretations drawn from this study and the prior observations of Gibbs, Merritt and Gibbs (1943). Differences in detail are believed to be due to the methods used for subdividing the types of seizures and the focal abnormalities of the electroencephalographic records.

2. Focal abnormality in focal epilepsy was almost invariably recorded over the hemisphere suspected on clinical grounds. Focal records were frequent (90.7 per cent among cases of hemiseizure, jacksonian seizures and adversive seizures). Focal abnormality related to the ipsilateral hemisphere in unilateral seizures was rare.

3. No invariable relation was discovered between the clinical estimate of the site of a lesion and the area covered by focally disordered activity in the electroencephalographic record.

4. More misses (i. e., normal or nonfocal records) were noted in cases of jacksonian march than in any other group.

5. When the case material for generalized convulsive seizures (with focal electroencephalographic abnormality), hemiseizures and jacksonian seizures was divided into age groups at the fourth and tenth birthdays, there was a definite increase in the incidence of slow focal patterns in the oldest age group.

6. There was the same variation in distribution of abnormal focal patterns in generalized seizures with and without convulsion. Neurologic localizing signs were very infrequent in the group without convulsions but occurred in 37 per cent of the cases in the group with generalized convulsions.

7. The same variety of abnormal patterns of the record between seizures was observed in all the classes of focal epilepsy studied, i. e., amplitude asymmetries, slow sequences, spike-waves and spikes. Each of these patterns could have been further subclassified without noting significant absences associated with any type of focal epileptic seizure.

8. When diffuse amplitude asymmetry is the outstanding difference between left-sided and right-sided combinations of leads, the high amplitude pattern generally occurs over the clinically suspected hemisphere.

9. An outstanding difference reported between jacksonian terminal and jacksonian march seizures was the low incidence of related evidence of neurologic abnormality in the former and the high incidence in the latter. The chance of electroencephalographic localization of abnormality in jacksonian terminal seizures exceeded that in jacksonian march seizures.

Staff physicians of St. Louis hospitals aided in the diagnoses in the cases studied. Technicians Rosemary Baessler and Rosemary Lambert assisted in the study.

VISUAL RETENTION TEST PERFORMANCE IN CHILDREN

Normative and Clinical Observations

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THE VISUAL retention test is a "memory for designs" test devised for use with adult patients as a measure of immediate memory capacity which would utilize sensorimotor components different from those of the familiar auditory-vocal digit span and which could thus serve as a valuable supplement to the digit span in the clinical examination. The visual retention test has enjoyed a fair amount of clinical use, and the question has been raised by several workers whether it might not be employed as a psychodiagnostic device with school children, as well as with adults. The discussion in the original paper [1] on the shortcomings of the digit span as a test of immediate memory and of the desirability of utilizing other types of tests in the evaluation of the immediate memory capacity of adult patients applies with equal force to the diagnostic problems presented by children. Moreover, a retention test the sensorimotor components of which are visuomotor in nature (rather than auditory-vocal, as in the digit span) has a quite definite place in the evaluation of the memory capacity of children suspected of having a brain injury. Such children frequently show a selective impairment in intellectual function; for example, verbal abilities may be relatively well developed, while visuoideational and visuomotor performances may be significantly impaired.[2] A clinical examination which neglects these

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1. Benton, A. L.: A Visual Retention Test for Clinical Use, Arch. Neurol. & Psychiat. **54**:212-216 (Sept.) 1945.

2. The study of R. K. Byers and E. E. Lord (Late Effects of Lead Poisoning on Mental Development, Am. J. Dis. Child. **66**:471 [Nov.] 1943) on children who had suffered from lead poisoning in early life and had been discharged from the hospital as "cured" is particularly instructive in this respect. Of 20 such children who had entered the school system, no less than 18 were doing extremely poorly in school. Only 4 of these 18 children had an intelligence quotient below 86, and thus a generally low mental level cannot be invoked as the cause of the school failure. However, psychologic examination of these children with adequate

visuopsychic factors may well yield a distorted and inaccurate picture of such a child's capacities either by overrating the true academic aptitude and adjustment capacity of a verbally well developed child who does have a visuopsychic disability or, conversely, by an unduly pessimistic appraisal of a child who by virtue of a cerebral lesion has a specific language disability.

These considerations made it seem worth while to make an exploratory investigation of the performances of school children on the visual retention test to determine whether the difficulty range of the test was such that it could be utilized clinically with children. These preliminary observations indicated quite clearly that the test was not too difficult for school children and that the older children (13 to 16 years of age) in general did about as well as do adults. In addition, observation of deviant performances suggested that failure on the test might be related to clinically and educationally significant behavioral deviations. Accordingly, a more extended normative and clinical study was undertaken, the results of which are reported here.

METHOD

The subjects whose performances served as basic data for a normative study to establish standards for different age levels were a group of 245 school children (127 boys and 118 girls), ranging in age from 8 to 16 years, the grade placement ranging from the third to the ninth grade. The children were attending two schools, selected because they were considered to draw students from neighborhoods which were fairly representative of the total population of Louisville. The performances of these 245 children (selected from a total group of about 350 children who were tested) were selected as basic data for standardization of the test because they met all the following criteria: (1) Their grade placement for their age was normal, i. e., it did not deviate more than one year from the standard age-grade placement; (2) their intelligence level, as measured by a group test of intelligence, was within normal limits (intelligence quotient 87 to 113); (3) their reading ability, as measured by the verbal portions of a group test of intelligence, was within normal limits (reading quotient, 87 to 113). The children on whom clinical observations were made were either patients referred by physicians to one of us (A. L. B.) for examination or children referred by

"general" intelligence (intelligence quotient 86 to 109) and with inadequate school achievement characteristically disclosed defective visual memory, form discrimination and visuomotor skill. "By contrast, many of the children showed normal or even superior abilities in the language field, and on this account several of the most severely handicapped children made relatively high scores on the Stanford-Binet tests. Such children were frequently socially responsive, especially in their preschool years, and were considered 'bright' by parents and teachers, the latter often stating that the children could do better if only they would try."

The recent paper of E. Meyer and M. Simmel (The Psychological Appraisal of Children with Neurological Defects, J. Abnorm. & Social Psychol. **42**:193, 1947) is likewise instructive in its demonstration of the multiple intellectual defects that may be shown by a child with a brain injury who has a "normal" intelligence level.

school principals to the other (N. T. C.) for examination because of a scholastic problem. In all cases the test was administered and scored according to the standard directions.[1]

NORMATIVE OBSERVATIONS

The performances of the school children on the visual retention test are presented in table 1, in which are given the distribution of the 245 individual scores and the mean score for each age level. It will be noted

TABLE 1.—*Distribution of Scores of 245 Children on the Visual Retention Test*

Age,* Years	Number of Subjects	Form	Score							Mean Score
			0	1	2	3	4	5	6	7	
8	7	A	..	2	..	3	2	..	..	..	2.71
	14	B	..	3	4	5	1	1	..	..	2.50
9	12	A	..	..	2	1	7	2	..	..	3.75
	11	B	..	1	2	4	2	2	..	..	3.18
10	14	A	..	..	1	2	5	4	2	..	4.29
	17	B	..	1	1	5	3	3	2	2	4.18
11	17	A	..	..	..	3	5	4	4	1	4.71
	21	B	..	..	1	1	6	5	6	2	4.95
12	21	A	..	..	1	1	4	4	8	3	5.24
	23	B	..	..	..	3	5	4	7	4	5.27
13	21	A	..	..	..	..	3	3	11	4	5.76
	14	B	..	..	..	1	1	3	6	3	5.60
14	15	A	..	..	..	..	1	4	7	3	5.87
	8	B	..	..	1	..	1	1	3	2	5.38
15-16	20	A	..	..	..	..	..	4	8	8	6.20
	10	B	..	..	..	..	2	2	5	1	5.50

* Age is stated to nearest birthday.

TABLE 2.—*Schema for Interpretation of Performance on the Visual Retention Test in Children*

Age,* Years	Defective	Subnormal ("Borderline")	Low Average	Average	High Average	Superior	Very Superior
8	0	1	2	..	3	4	5-7
9	0-1	2	3	..	4	5	6-7
10	0-2	..	3	4	5	6	7
11	0-2	3	4	..	5	6	7
12	0-2	3	4	5	6	7	...
13-16	0-3	4	5	6	7	..	...

* Age to nearest birthday.

that there was a steady increase in both the mean and the median score with age. Definitely poor performances (score under 4), as judged by the standards for adult subjects, became increasingly rare at the older age levels. For example, there were only 2 defective performances in the group of 88 subjects within the 13 to 16 year age range and no defective performances in the group of 30 subjects in the 15 to 16 year age range. On the other hand, at the youngest age levels, there were few performances which would be designated as average (score 6 or 7), as judged by the standards for adult subjects. In the group of 75 subjects

within the 8 to 10 year age range there were only 6 "average adult" performances, all of them achieved by the 10 year old children and none by the 8 or 9 year old children. With further increase in age there was, of course, a greater frequency of "average adult" performances. Table 1 also indicates that with children, as with adults, forms A and B of the test are approximately equal in difficulty level.

In table 2 is presented a schema for the interpretation of the performances of children on the visual retention test which is based on these normative data and which we have found useful in clinical practice.

CLINICAL OBSERVATIONS

Retarded Children.—In a group of 30 unselected children with significant retardation in general intelligence (intelligence quotient 58 to 81), it was found that a majority made relatively poor performances on the test, their scores being in consonance with their mental age rather than with their chronologic age. The median chronologic age for this group of children was 12 years 10 months; the median mental age was 9 years 5 months; the median intelligence quotient was 77 and the median score on the visual retention test was 3, corresponding to an age level of about 8½ years. Nevertheless, 7 of the children made scores on the visual retention test significantly higher than their general mental level. On the other hand, there were no less than 7 children whose performances on the visual retention test were significantly poor even in relation to their low mental ages. Detailed histories of these children are not available, and therefore it is not possible to determine whether these strikingly poor performances show a special correlation with the occurrence of acquired damage to the brain.

Superior Children.—In a group of 32 children with significant acceleration in mental development (intelligence quotient 119 to 143), it was found that a majority made relatively good performances on the test, their scores being in consonance with their mental age rather than with their chronologic age. The median chronologic age for this group of children was 9 years 8 months; the median mental age was 12 years 2 months; the median intelligence quotient was 125, and the median score on the visual retention test was 5, corresponding to an age level of about 12 years. Nevertheless, 10 of the 32 children made relatively poor performances, the level of performance being significantly below the general mental level and in 1 case being below even the chronologic age level.

Children with Reading Disabilities.—In a group of 13 children of adequate intelligence who showed a retardation in the development of reading skills which was adversely affecting school progress, it was found that the performances of these children on the visual retention test

showed no significant deviation, only 1 of the group making a clearly subnormal performance. The median chronologic age for this group of children was 10 years 7 months; the median intelligence quotient was 98, and the median score on the visual retention test was 4, corresponding to an age level of about 10 years.

Children with Brain Injury.—In a group of 14 children with brain injuries whose general intelligence level was within broad normal limits (intelligence quotient 82 or greater), it was found that 7 showed significantly subnormal performances on the visual retention test (below low average level) for their age level. Three children made low average performances, and 4 children made average performances. No child made a high average or superior performance in relation to his age level. In comparison, it may be noted that our experience has been that the performance on the Goodenough "drawing a man" test is also significantly defective for about half the children with brain injuries whose general intelligence level is within broad normal limits. Defective performances on the two tests are usually, but not always, made by the same children. About two thirds of the children with brain injuries whose general intelligence is fair make defective performances on one or the other test. Stated in another way, in our experience, about one third of children of fair general intelligence with reasonably well established evidence of brain injury (history, neurologic examination, evaluation of general behavior) do not make defective performances on either test.

COMMENT

The normative data seem quite clear in their indications that the visuopsychic function (immediate visual memory with graphic response) as assessed by the visual retention test is in a state of growth through the age range of 8 to 14 years and that the level of efficiency attained by a child in respect to this function can be gaged by the test. The data on retarded and accelerated children show that the ability is fairly closely correlated with the level of general intelligence. Nevertheless, that this visuomotor function is to be distinguished from the verbal type of intelligence usually designated as "general" intelligence is indicated by the variations found in the different groups of children. Thus, while superior children generally do very well on the test, a number of these children do relatively poorly, suggesting that their intellectual superiority is along verbal symbolic lines rather than completely general in nature. Again, the occurrence of good performances among the retarded children suggests that the intellectual deficits of these children may be concentrated in the academically important verbal symbolic area and may not be as general as might be assumed from, for example, their performances on

the Stanford-Binet or on group intelligence tests. Finally, the fact that about 50 per cent of children with brain injuries who are of adequate "general" intelligence make defective performances on the test points to the specific character of the ability assessed by the test.

In this regard, the usefulness of the visual retention test as an instrument to secure a fuller picture of the mental equipment of any child, whether he is suspected of having a brain injury or not, suggests itself. In the superior child performance on the visual retention test may indicate whether the superiority extends to vocationally important nonverbal areas of intellectual function, as well as to the usual verbal symbolic areas. In the retarded child performance on the visual retention test may indicate whether training along certain nonacademic lines offers fruitful possibilities.

The finding that children with reading disabilities do not deviate from the norm in respect to performance on the visual retention test supports the view that this language deficit is highly specific and that its determinants are not to be found in brain injury in the usual sense of the term. It is true that many children with brain injuries encounter special difficulty in learning to read, and, in relation to their general intellectual level, it is often justifiable to consider them as having a "reading disability." But it would be fallacious to extend this reasoning to the converse situation, for there is little evidence that the occurrence of a reading disability per se carries with it any strong suggestion that a brain injury will be found.

The visual retention test succeeds in identifying about 50 per cent of children of fair general intelligence who have brain injuries and presumably points to selective damage to the brain in these patients. Among the retarded children there were several whose performances on the visual retention tests were grossly defective, significantly lower than their relatively low mental ages. Unfortunately, it was not possible to examine these children or to secure histories on them to determine whether they showed specific evidence of brain injury. In view of the predilection of children with brain injuries and fair general intelligence to do poorly on the visual retention test, it is quite possible that the abnormally poor performances among the mentally defective children was indicative of selective damage to the brain. This is a question which deserves further exploration.

The fact that in general the child whose performance on the visual retention test is defective will also do poorly on the Goodenough "drawing a man" test points to the common functions assessed by the two tests. Both call for visuomotor or, more specifically, "visuographic" performances. The visual retention test adds to this an immediate

memory factor, while in the Goodenough test, according to Bender,[3] the ideational factor of the child's concept of the body image is involved. In the case of patients who do well on the visual retention test and poorly on the "drawing a man" test, one might conclude that immediate visual memory is intact but that the concept either of one's own body or of the human figure in general is impaired and might draw whatever inference concerning localization seems warranted. In patients who do poorly on the visual retention test and adequately on the "drawing a man" test, the immediate visual memory factor per se may be implicated. For example, a boy of 9 years, in the early stages of a cerebral degenerative disorder (in all probability Schilder's disease) completely failed the visual retention test, Form A. The absolute inability to reproduce correctly any of the designs led the examiner to consider the possibility either of a graphomotor incapacity or of a decisive visual disturbance, although neither seemed likely from the evidence of other test performances, reading, etc. The child was asked to *copy* the designs of visual retention test, Form B. He copied the designs fairly well. His performance on the "drawing a man" test was excellent, being equivalent to his chronologic age level and above his obtained mental age level. In this patient the visual retention test apparently disclosed an immediate visual memory defect (such as has been observed in patients with lesions of the occipital lobe), which could not have been made evident by the "drawing a man" test. In general, it would seem that the use of the two tests in combination offers fruitful possibilities not only for the detection of the presence of brain injury in a child but also for the analysis of specific deficits.

SUMMARY

A normative study of the performances on the visual retention test of children within the age range of 8 to 16 years indicates that the test is not too difficult for children in this age range and is a convenient instrument for assessing the immediate visual memory function in children. Normative standards of performance for the different age levels have been developed on the basis of the standardization data.

Observation of the performances on the visual retention test of children with retarded or accelerated mental development indicates that there is in general a fairly close correlation between performance on the visual retention test and mental age (rather than chronologic age). Discrepancies in performance levels between the visual retention and the verbal intelligence test may have clinical significance.

3. Bender, L.: The Goodenough Test (Drawing a Man) in Chronic Encephalitis in Children, J. Nerv. & Ment. Dis. **91**:277-286, 1940; Organic Brain Conditions Producing Behavior Disturbances, in Lewis, Nolan D. C., and Pacella, B. L.: Modern Trends in Child Psychiatry, New York, International Universities Press, 1945, pp. 155-192.

Observation on the performances on the visual retention test of children with brain injuries who are of adequate "general" intelligence indicates that about half such children make defective performances on this test. Comparison of the performances of the same children on the visual retention test and on the Goodenough "drawing a man" test suggests that the use of both tests with children suspected of having a brain injury offers fruitful possibilities both for detection of the presence of damage to the brain and for analysis of the extent of such damage.

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EXTRACELLULAR FLUID AND PLASMA VOLUMES IN DEPRESSED PATIENTS GIVEN ELECTRIC SHOCK THERAPY

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IT HAS LONG been known that patients with depressions usually exhibit rapid gain in weight in association with, or preceding the onset of, spontaneous remissions. A similar gain in weight is usually noted in patients who improve during the course of electroconvulsion therapy, although in some of them a small initial loss is not uncommon. In patients who show a rapid gain in weight in association with electroshock, the increase usually amounts to 3 to 5 pounds (1.3 to 2.3 Kg.) accumulated over a period of three or four days. At times larger increases may occur; in an extreme instance seen at this hospital a patient gained 14 pounds (6.4 Kg.) in seventy-two hours. Occasionally edema of the ankles may be noted. The rapidity of the gain and the occasional appearance of edema made it clear that much of the gain must be consequent to water retention. Accordingly, it was considered desirable to undertake the present study.

MATERIAL AND METHODS

Twelve depressed patients, ranging in age from 36 to 72 years, were studied; 9 were women. The diagnosis indicated in the table varied. All studies were made with the patient in a basal state one to three days after the last treatment. The patients were weighed on the day of each study. Complete studies were made in 9 cases, while in 3 only the extracellular fluid volume was measured. The following procedure was used: (1) Ten cubic centimeters of blood was taken. The serum served as the blank for the thiocyanate determination. The needle was left in place, and (2) 15 cc. of a solution containing 512 mg. of sodium thiocyanate was injected intravenously. (3) Fifteen cubic centimeters of blood was taken ninety minutes later. The serum was divided into two portions, one for determination of thiocyanate and the other to serve as a blank for the estimation of plasma volume. The needle was left in place and (4) 10 cc. of T 1824 solution (Evans blue) was injected intravenously; a stopwatch was started at this time. (5) Ten cubic centimeters of blood was taken ten or fifteen

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minutes later, the time being noted accurately. (6) Three additional samples of 10 cc. each of blood were taken at intervals of approximately five minutes, the time being noted accurately in each case.

The plasma volume was calculated by the method of Gibson and Evans [1] from data obtained by measurements of the optical density of plasma samples containing dye by means of a Coleman Junior spectrophotometer. The extracellular fluid volume was calculated by means of the method of Crandall and Anderson [2] using their formula A. The estimation of plasma thiocyanate was performed as follows: *(a)* One cubic centimeter of serum was added, with shaking, to 4 cc. of 10 per cent trichloroacetic acid in a centrifuge tube. *(b)* The mixture was centrifuged at 2,000 revolutions per minute for seven minutes. *(c)* Three cubic centimeters of the supernatant fluid was mixed with 3 cc. of the thiocyanate reagent. *(d)* At the end of ten minutes the intensity of the color was measured in a Coleman Junior spectrophotometer at a setting of 475 angstrom units, using as a blank 3 cc. of reagent mixed with 3 cc. of a 4:1 mixture of 10 per cent trichloroacetic acid and isotonic saline solution.

The validity of the thiocyanate method for the estimation of extracellular fluid volume has been studied by a number of workers. Kaltreider and co-workers [3] found good agreement in human subjects between the thiocyanate and the radioactive sodium methods. In dogs, however, Winkler, Elkinton and Eisenman [4] found no such agreement, a divergence possibly explainable on the basis of species differences. However, both of these groups, and also Ashworth and co-workers,[5] found that the thiocyanate method showed changes in extracellular fluid volume accurately. Kaltreider and co-workers [3] concluded that a period of three hours after the injection of thiocyanate was required for equilibration in nonedematous subjects; this conclusion is in contrast to that of all other workers,[6] who found that one hour was adequate. An objection to allowing a long period for equilibration is

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2. Crandall, L. A., Jr., and Anderson, M. X.: Estimation of the State of Hydration of the Body by the Amount of Water Available for the Solution of Sodium Thiocyanate, Am. J. Digest. Dis. **1**:126, 1934.

3. Kaltreider, N. L.; Meneely, G. R.; Allen, J. R., and Bale, W. F.: Determination of the Volume of the Extra-Cellular Fluid of the Body with Radioactive Sodium, J. Exper. Med. **74**:569, 1941.

4. Winkler, A. W.; Elkinton, J. R., and Eisenman, A. J.: Comparison of Sulfocyanate with Radioactive Chloride and Sodium in the Measurement of Extra-Cellular Fluid, Am. J. Physiol. **139**:239, 1943.

5. Ashworth, C. T.; Muirhead, E. E.; Thomas, O. F., and Hill, J. M.: An Analysis of the Thiocyanate Method for Determining the Distribution of the Body Fluids, Am. J. Physiol. **134**:255, 1943.

6. Lavietes, P. H.; Bourdillon, J., and Klinghoffer, K. A.: The Volume of the Extra-Cellular Fluids of the Body, J. Clin. Investigation, **15**:261, 1936. Crandall and Anderson.[2] Winkler, Elkinton and Eisenman.[4] Ashworth, Muirhead, Thomas and Hill.[5]

that the excretion of thiocyanate into urine and into gastrointestinal secretions may become large enough to introduce errors in the method; in addition, thiocyanate disappears from the blood in a manner not understood and at rates which might introduce significant present errors after several hours.[5] Accordingly, a period of ninety minutes was allowed in the present study. Although Ashworth and associates [5] concluded that plasma thiocyanate concentrations of approximately 8 mg. per hundred cubic centimeters were optimal for making the measurements, it was considered that lower concentrations, i. e., 3.5 to 5.0 mg.

Changes in Weight and in Extracellular Fluid and Plasma Volumes in Depressed Patients Given Electroconvulsion Therapy

Case	Age	Sex	Weight, Kg.	Extracellular Fluid Volume, L.	Plasma Volume, L.	Treatments, Number	Diagnosis
1	63	M	62.3	13.47	2.35	0	Manic-depressive psychosis, depressed
			66.8	16.51	....	6	
			70.5	16.01	3.08	13	
2	63	M	67.8	15.06	3.05	0	Manic-depressive psychosis, depressed
			68.2	17.07	3.58	6	
3	48	M	66.1	15.28	2.62	0	Manic-depressive psychosis, depressed
			66.8	16.00	3.03	3	
4	36	F	48.7	12.37	2.12	0	Manic-depressive psychosis, depressed
			47.5	11.69	2.13	9	
5	53	F	53.0	12.19	2.03	0	Manic-depressive psychosis, depressed
			53.0	11.91	....	3	
6	40	F	46.0	10.72	....	0	Manic-depressive psychosis, depressed
			48.2	12.14	....	9	
7	32	F	50.9	10.5	....	0	Manic-depressive psychosis, depressed
			52.3	12.8	....	6	
8	59	F	46.4	9.85	1.86	0	Involutional psychosis—melancholia
			48.2	11.38	1.91	6	
9	61	F	68.6	12.19	2.14	0	Involutional psychosis—melancholia
			70.5	13.84	2.44	5	
10	61	F	55.9	12.32	2.46	0	Involutional psychosis—melancholia
			56.8	13.68	2.61	9	
11	72	F	41.4	9.76	....	0	Involutional psychosis—melancholia
			45.0	11.92	....	9	
12	30	F	52.7	10.75	2.18	0	Psychoneurosis—reactive depression
			52.3	11.13	....	3	
			52.3	10.25	2.00	5	

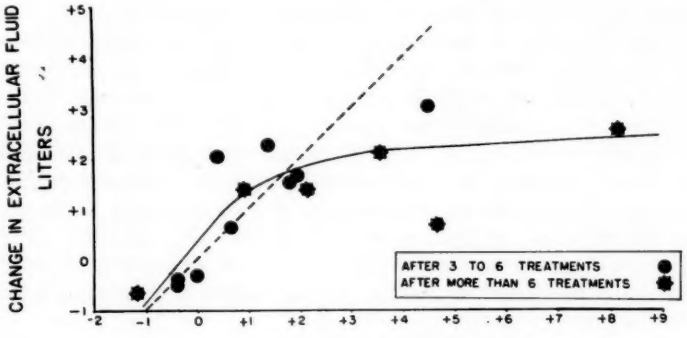
per hundred cubic centimeters, could be safely used with the precise photoelectric methods used here; errors due to more rapid disappearance of thiocyanate from the plasma at high plasma levels were thereby avoided.

OBSERVATIONS

Before treatment, the extracellular fluid volume was between 9.76 and 15.28 liters, or 17.8 and 25.4 per cent of the body weight. The extracellular fluid volume rose in the 9 patients who gained weight during the course of therapy. The 3 remaining patients gained no weight during the period of study (2 gained later with further therapy); none of these showed an increase in extracellular fluid volume (the

table and chart). When studies were made after three to six treatments, changes in weight in kilograms were equal to changes in extracellular fluid volume in liters. When, however, studies were made after nine or more treatments, gains in weight were large and increases in extracellular fluid volume were usually not great enough to account for the gains in weight (cases 1, 3 and 11 in the table; also the chart).

The plasma volume was between 1.86 and 3.05 liters before treatment, and in the patients who gained weight it was between 1.91 and 3.58 liters during or after the course of therapy (the table). The increases ranged between 50 and 730 cc., or 2.7 and 31.0 per cent of the initial value; the average increase was 362 cc., or 14.5 per cent. The 3 patients who gained no weight during the period of study (cases 4, 5 and 12 in the table) showed no change in plasma volume.



Changes in weight and in extracellular fluid volume during the course of electric convulsion therapy in patients with depressions. The dotted line is the one close to which all points should fall if the gain in weight were consequent entirely on gain in extracellular water. The solid line represents the relationship actually found.

COMMENT

The patients of the present study had values for extracellular fluid before treatment equal to 17.8 to 25.4 per cent of body weight; indeed, only 1, a patient in whom the depression was so mild as to arouse discussion as to the diagnosis, had a value above 23.6 per cent. The values found before treatment are therefore in the lower part of the range found in normal subjects by Kaltreider and co-workers,[3] Crandall and Anderson [2] and also workers in these laboratories.

The gain in weight which occurs in association with the onset of improvement during electric shock therapy is accompanied with an increase in the volume of the extracellular fluid as measured by the thiocyanate method. The observation of Trolle [7] that a diminution

7. Trolle, C.: Studies of the Water Excretion in Recovery from Maniac-Depressive Psychosis (Depressive Phase), Acta psychiat. et neurol. **20**:235, 1945.

in the volume of urine excreted occurred when depressed patients on a fixed water regimen began to improve is of interest in this regard, although that author did not take into account other sources of water loss. The extracellular fluid volume, initially in or slightly below the lower normal range, does not increase to levels above the normal. Small increases in plasma also occur. With small increases in weight early in the course of electricconvulsion therapy, the weight of the extracellular fluid gained is not significantly different from the gain in weight exhibited by the patient as a whole. After a longer course of shock therapy, however, the gain in extracellular fluid volume is less than the gain in weight and it therefore appears that new protoplasm is formed at this time. Studies of nitrogen balance which might throw light on the latter conclusion are not available, although Schou and Trolle [8] did find a positive nitrogen balance in patients given convulsion therapy by means of pentamethylenetetrazol (metrazol®).

Evidence exists of increased excretion of adrenal cortex hormone after electrically induced convulsions [9]; the findings of the present study are consistent with the effects of the action of some steroid hormones. It is unlikely that changes in body water content per se are causally related to the clinical improvement which is associated with electricconvulsion therapy; administration to depressed patients of desoxycorticosterone or progesterone, steroid hormones which may cause retention of salt and water, has no beneficial effect.[10] These findings do not rule out the possibility that some other action of steroid hormones is the factor responsible for the remission of mental disease effected by electroconvulsion therapy.

SUMMARY AND CONCLUSIONS

The extracellular fluid volume is in the lower normal range in patients with depressions. The rapid gain in weight which occurs in

8. Schou, H. I., and Trolle, C.: The Nitrogen Balance in Patients Suffering from Melancholia, Acta psychiat. et neurol. **16**:243, 1941.

9. Altschule, M. D.; Cram, J. E., and Tillotson, K. J.: Fall in Plasma Protein Level Associated with Rapid Gain in Weight During the Course of Electroshock Therapy, Arch. Neurol. & Psychiat., **59**:476, 1948. Altschule, M. D., and Tillotson, K. J.: Effects of Electroconvulsive Therapy on Diuretic Response to Water in Psychotic Patients, Arch. Neurol. & Psychiat. **61**:188, 1949. Altschule, M. D.; Altschule, L. H., and Tillotson, K. J.: Changes in Blood Leukocytes in Man After Electrically Induced Convulsions, to be published. Altschule, M. D.; Parkhurst, B. H., and Tillotson, K. J.: Decrease in Blood Eosinophilic Leukocytes After Electrically Induced Convulsions, J. Clin. Endocrinol. **9**:440, 1949. Mikkelsen, W. P., and Hutchens, T. T.: Lymphopenia Following Electrically Induced Convulsions in Male Psychotic Patients, Endocrinology **42**:394, 1948.

10. Altschule, M. D., and Tillotson, K. J.: Effect of Electroconvulsive Therapy on Water Metabolism in Psychotic Patients, Am. J. Psychiat., **105**:829, 1949.

such patients during the course of electricconvulsion therapy is accompanied with an increase in extracellular fluid volume. When small amounts of weight are gained, there is no significant difference between the weight of the extracellular water gained and the increase in weight of the patient; when larger amounts of weight are gained, the increase in extracellular water is not large enough to account for the increase in body weight. The plasma volume shows small and usually insignificant changes in the same direction as those of the extracellular fluid volume. The findings are consistent with the effects of the action of some steroid hormones.

CHANGES IN LEUKOCYTES OF THE BLOOD IN MAN AFTER ELECTRICALLY INDUCED CONVULSIONS

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THE WORK of Dougherty and White [1] and others has established the fact that lysis of circulating lymphocytes is under the hormonal control of the adrenal cortex. In view of the evidence that electrically induced convulsions change the rate of formation of steroid hormones in patients with mental disease,[2] it was considered of interest to study the number of circulating lymphocytes and other leukocytes before and after such seizures.

MATERIAL AND METHODS

The subjects were 13 patients ranging in age from 19 to 71 years; 11 were women. The diagnoses varied. Four patients were studied from three to six times each, and 9 were studied once each. Patients studied during treatments which numbered eleven or fewer were being given shock therapy three times a week; the others, studied on the occasion of the twelfth to the fifty-fourth shock, were receiving treatments at five or seven day intervals at the time the observations were made.

The patients were brought to the treatment room fourteen hours after their last meal. Blood was drawn from an antecubital vein one to three minutes before the induction of the seizure and again one-half hour and three hours after it. The total number of leukocytes was counted in samples of this blood, two pipets being used for each sample; differential white blood cell counts were also made, 500 cells being counted each time. The figures for polymorphonuclear leukocytes includes those for filamented and nonfilamented neutrophils, eosinophils and basophils.

From the Clinical Services and the Laboratory of Clinical Physiology, McLean Hospital, Waverley, Mass., and the Departments of Medicine and Psychiatry, Harvard Medical School.

1. Dougherty, T. F., and White, A.: Evaluation of Alterations Produced in Lymphoid Tissue by Pituitary Adrenal Cortical Secretion, J. Lab. & Clin. Med. **32**:584, 1947.

2. Hoagland, H.; Malamud, W.; Kaufman, J. C., and Pincus, G.: Changes in the Electroencephalogram and the Excretion of 17-Ketosteroids Accompanying Electroshock Therapy of Agitated Depression, Psychosom. Med. **8**:246, 1946. Altschule, M.D., and Tillotson, K. J.: To be published.

OBSERVATIONS

Immediately before the convulsion the leukocyte counts ranged from 4,750 to 14,500 per cubic millimeter of blood, the average being 10,064 per cubic millimeter. One-half hour after the seizure the counts were slightly lower in 19 instances and higher in 6 instances; the range of change was from + 4,250 to — 3,100 cells and averaged — 432 cells per cubic millimeter. The percentage change ranged from — 29

Changes in Leukocyte Count of the Blood Induced by Electric Shock Treatments in 13 Patients

Case No.	Age, Yr.	Sex	Treatment No.	Leukocytes, per Cu. Mm.			Polymorphonuclear Cells, per Cu. Mm.			Lymphocytes, per Cu. Mm.			Comment
				Before	½ Hr.	3 Hr.	Before	½ Hr.	3 Hr.	Before	½ Hr.	3 Hr.	
1	71	M	1	14,500	13,150	14,150	11,195	10,410	12,085	2,650	1,920	1,445	Involutional psychosis (melancholia); patient had 5 shocks 20 mo. previously
			3	11,000	10,400	13,900	8,360	8,510	12,260	1,805	1,125	1,640	
			5	11,900	10,750	12,450	9,330	8,900	10,460	1,715	1,335	1,395	
			7	11,000	10,250	14,250	8,280	8,800	12,000	2,140	820	1,340	
			9	13,000	11,500	15,650	10,115	9,490	13,520	1,870	1,495	1,220	
			11	11,250	10,800	13,550	8,680	8,660	11,350	1,825	1,295	1,575	
2	19	F	1	8,450	8,250	9,900	6,000	6,600	8,515	2,080	1,370	1,090	Schizophrenia, catatonic; patient recently had 8 wk. of ambulatory insulin therapy; had 7 shocks 14 mo. previously
			3	7,750	6,700	9,200	5,360	4,940	7,550	1,940	1,325	1,160	
			5	10,350	7,250	11,000	7,900	5,770	9,990	2,200	1,245	925	
			7	9,350	9,250	10,200	7,260	7,260	8,810	2,095	1,610	1,140	
3	54	M	1	10,200	12,350	16,700	6,620	8,560	15,030	2,445	2,495	1,235	
			3	8,700	8,750	14,900	5,830	6,215	11,165	2,335	1,855	1,520	
			5	11,250	10,700	13,250	8,080	7,530	10,550	2,295	2,055	1,775	
4	61	F	1	4,750	9,000	13,450	2,830	6,175	11,740	1,690	2,430	1,020	Involutional psychosis (melancholia)
			3	8,950	7,600	10,350	5,640	4,870	8,920	3,200	2,400	1,140	
			5	11,000	10,750	12,900	7,460	7,620	10,800	2,880	2,715	1,495	
5	69	F	7	7,500	5,350	8,800	5,850	4,655	7,145	1,425	600	1,435	Involutional psychosis (melancholia)
6	22	F	12	7,000	6,400	.....	3,240	3,790	.....	3,515	2,140	.....	Epilepsy with schizophrenia; patient had 12 shocks 10 mo. previously
7	44	F	14	14,450	13,350	12,300	11,725	10,280	9,545	2,185	2,375	2,265	Manic-depressive psychosis, mixed; patient had 12 shocks 18 mo. previously
8	45	F	17	10,650	11,350	11,350	8,690	9,665	9,350	1,620	1,385	1,475	Schizophrenia, paranoid; patient had 18 shocks 2 yr. ago. and 5 14 mo. previously
9	48	F	17	9,600	10,200	10,850	6,585	6,795	9,030	2,690	2,775	1,325	Cerebral atrophy with psychosis, paranoid
10	49	F	33	13,500	12,300	12,350	10,830	10,450	9,460	2,455	1,375	2,395	Schizophrenia, paranoid
11	68	F	34	8,400	6,800	6,300	6,450	5,360	5,810	1,780	1,185	265	Involutional psychosis (melancholia); patient had 40 shocks in 2 yr. up to 2 yr. previously
12	49	F	36	8,650	7,800	13,500	6,280	5,925	11,610	1,060	1,310	1,325	Schizophrenia, paranoid
13	58	F	54	8,350	8,750	11,650	5,430	6,295	8,970	2,340	1,610	2,025	Manic-depressive psychosis, manic phase; patient had 9 shocks 2 yr. previously

to + 89 of the control values, but in only 1 case was it above + 21, the average percentage change being — 1.6. At the end of three hours the counts were raised in 20 instances and decreased below the control levels in 4 instances; the range of change was + 6,500 to — 1,900 cells, with an average of + 2,060 cells per cubic millimeter. The percentage change ranged from + 184 to — 23 of the control values, with an average percentage change of 25.4.

Before the convulsion the range of polymorphonuclear cell counts was between 2,830 and 11,725 cells per cubic millimeter of blood, the average being 7,360 cells per cubic millimeter. At the end of one-half hour after the seizure the counts had fallen in 12, risen in 11 and remained unchanged in 2 instances; the range of change was from + 3,340 to — 2,130 cells, the average being — 19 cells per cubic millimeter. The percentage change ranged from + 118 to — 27, in all but 1 case the value lying between ± 30 per cent; the average percentage change was + 3.5. Three hours after the seizure the counts were higher than the control values in 21 instances and lower in 3; the range of change was from + 8,910 to — 2,280 cells, with an average of + 2,667 cells per cubic millimeter. The percentage change ranged from + 311 to — 20, with an average of + 47.8. The polymorphonuclear cell count was higher three hours after the seizure than one-half hour after it in all but 2 instances.

Before the convulsion the lymphocyte counts were between 1,425 and 3,515 cells per cubic millimeter of blood, the average being 2,200 cells. One-half hour after the seizure the lymphocyte counts had fallen in 21 instances and risen in 4 instances; the range of change was from — 1,375 to + 740 cells, with an average of — 503 cells per cubic millimeter. The percentage change ranged from — 62 to + 44, in only 1 instance being above + 9; the average change was — 23.1 per cent. Three hours after the convulsion the counts were lower than the control values in 22 instances and higher in 2 instances; the range of change was from — 2,060 to + 80 cells, with an average of — 733 cells per cubic millimeter. The percentage changes ranged from — 79 to + 4, with an average of — 32.3. At the end of three hours the lymphocyte counts were lower than those found one-half hour after the convulsion in 15 of 24 instances, being higher in the other 9 cases. In only 1 instance (case 7) was there no fall in the lymphocyte count at any time, the changes found being increases of 9 and 4 per cent at one-half and three hours, respectively.

The age and sex of the patient, the type of psychosis, the number of previous treatments and the stage of remission at the time of the studies did not influence the degree of morphologic change observed in the leukocytes of the blood.

COMMENT

The data from the present study show that after electrically induced convulsions in patients of different ages, of either sex and with various types of psychoses the following significant morphologic changes occur in the leukocytes of the blood:

1. A rise in the total leukocyte and in the polymorphonuclear leukocyte count three hours after the seizure.

2. An immediate and usually sustained fall in the lymphocyte count; a change in the character and magnitude which may possibly be significant in the data presented is a slight initial fall in the total leukocyte count. The decrease in the number of circulating lymphocytes resulting from electrically induced seizures may be interpreted as evidence of lysis

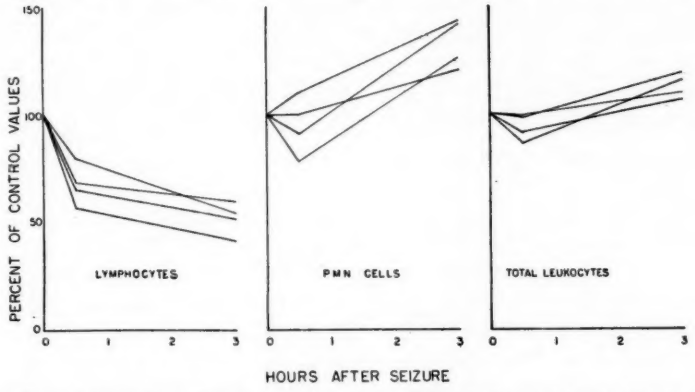

Chart 1 (case 2).—Changes in absolute number of leukocytes in the blood in a patient showing a sustained decrease in the lymphocyte count after electric shock.

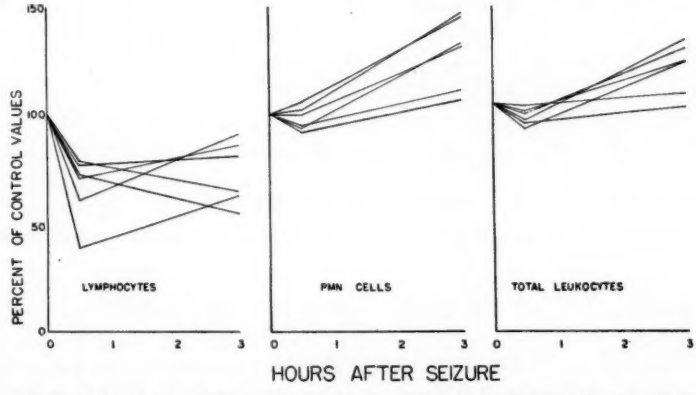

Chart 2 (case 1).—Changes in absolute number of leukocytes in the blood in a patient showing a variable duration of decrease in the lymphocyte count after electric shock.

of lymphoid structures; presumably, the late increase in polymorphonuclear cells represents a response to the presence of products of cellular breakdown in the circulation. The data indicate that the lysis of lymphocytes continues at least three hours after the end of the induced convulsion.

Earlier workers have also made observations on changes in the leukocytes of the blood in patients receiving electric shock therapy. The report of Centini and Bandettini di Poggio [3] is difficult to evaluate because absolute numbers of cells are not recorded and the counts were made fifteen minutes and again two days after the convulsions. In view of the fact that hemoconcentration exists during the first fifteen minutes, and often longer, after the seizure, it is clear that counts made too soon after the convulsion would yield false values. Counts made two days later would have little value in the present discussion. Similarly, the data of Katzenelbogen and associates [4] are presented with no

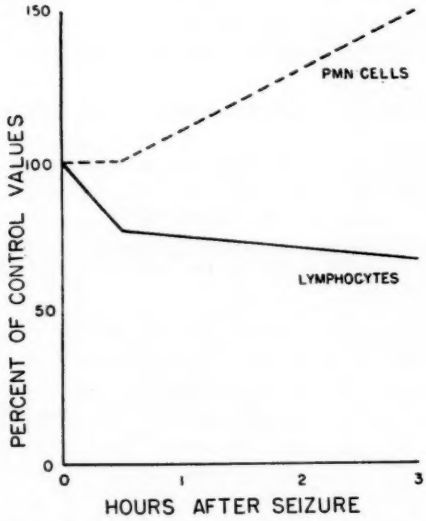

Chart 3.—Average changes in the blood leukocyte count after electric shock in 25 experiments.

regard to the time the blood counts were made relative to the convulsions except that all were made "within an hour"; moreover, the findings are published in a form which does not permit the evaluation of changes in the absolute numbers of various types of cells in the blood. Previously published data are, therefore, not helpful in regard to the present problem.

3. Centini, D., and Bandettini di Poggio, A.: Richerche biochimiche in schizofrenici durante l'elettroshock, Rassegna di studi psichiat. **28**:875, 1939.

4. Katzenelbogen, S.; Baur, A. K., and Coyne, A. R. M.: Electric Shock Therapy: Clinical, Biochemical and Morphologic Studies, Arch. Neurol. & Psychiat. **52**:323 (Oct.) 1944.

The pattern of changes in the blood observed in the present study is similar to that described by Dougherty and White [1] as occurring as a result of the action of adrenal cortex hormones. It is of interest in this regard that changes in the plasma protein concentration,[5] in extracellular fluid volume [6] and in ketosteroid excretion [2] during the course of electric shock therapy are also consistent with the action of steroid hormones. Although the present study is significant in that it supports the concept that stimulation of the adrenal cortex is a consequence of electrically induced convulsions, it does not determine whether the action of electric shock therapy is on the anterior lobe of the pituitary gland or directly on the cortex of the adrenal gland, nor does it make the mechanism of either of these possible effects clear. The findings also suggest that the liberation of the products of lysis of approximately 5,000,000,000 lymphocytes in the circulation, and probably several times that number in the tissues, after each electrically induced convulsive seizure might influence protein metabolism.

The relation of these and of previously observed physiologic changes to the therapeutic effects of electric convulsion therapy is unknown; it must be concluded, however, that the nature of some of the metabolic changes associated with clinical improvement is consistent with the effects of increased secretion of adrenal cortex hormones. The results here recorded suggest that the metabolic changes which occur together with improvement have their origin in the induced seizures but have their major action afterward.

SUMMARY AND CONCLUSIONS

After electrically induced convulsions in psychotic patients a rapid and sustained fall in blood lymphocytes develops; late rises in polymorphonuclear cells and in the total leukocyte count also occur. The changes observed are consistent with the effects of increased secretion of adrenal cortex hormones.

McLean Hospital.

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5. Altschule, M. D.; Cline, J. E., and Tillotson, K. J.: Fall in Plasma Protein Level Associated with Rapid Gain in Weight During the Course of Electroshock Therapy, Arch. Neurol. & Psychiat. **59**:476 (April) 1948.

6. Altschule, M. D.; Ascoli, I., and Tillotson, K. J.: Extracellular Fluid and Plasma Volumes in Depressed Patients Given Electric Shock Therapy, Arch. Neurol. & Psychiat., this issue, p. 618.

SIGNIFICANCE OF MATERNAL BEREAVEMENT BEFORE AGE OF EIGHT IN PSYCHIATRIC PATIENTS

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IN A PREVIOUS study[1] evidence was presented which indicated that death of the mother during childhood was more likely to be related to subsequent psychosis than death of the father. The incidence of maternal deaths was three times as great among psychotic persons as among normal controls (15.7 versus 5.3 per cent); the incidence of paternal deaths, on the other hand, was approximately equal among the psychotic and the normal persons (11.1 and 10.0 per cent). The ratio of maternal to paternal deaths is a useful measure, since mortality rates vary widely both from decade to decade and according to social and economic status in any given year. Thus, in the general population the normal expectancy is that two fathers will die for every mother that dies. The reason for the preponderance of paternal deaths is that mortality rates are higher for males than for females at all ages and that husbands are older than their wives. Among parents of psychotic persons it was found that three mothers died during the patient's childhood for every two fathers who died. The disproportionate number of mothers of psychotic persons who died during the patient's childhood (nearly three times the anticipated number) would seem to warrant more detailed investigation.

While there have been numerous studies on the traumatic effect of parental death that are based on the method of individual case studies,[2] and while statistical data have been presented on the frequency of bereavement in relation to such states as delinquency[3] and ulcerative colitis,[4] there have been relatively few attempts to study the precise incidence of parental deaths among psychotic patients. Rosenzweig and

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1. Barry, H., Jr.: A Study of Bereavements: An Approach to Problems in Mental Disease, Am. J. Orthopsychiat. **9**:355, 1939.

2. Bender, L., and Schilder, P.: Suicidal Preoccupations and Attempts in Children, Am. J. Orthopsychiat. **7**:225, 1937.

3. Glueck, S., and Glueck, E. T.: Five Hundred Delinquent Women, New York, Alfred A. Knopf, Inc., 1934.

4. Lindemann, E.: Psychiatric Aspects of Conservative Treatment of Ulcerative Colitis, Arch. Neurol. & Psychiat. **53**:322 (April) 1945.

Bray [5] have presented some figures. However, their series involved a selective factor, since they were primarily interested in sibling deaths, and they included only cases in which precise data on this point were obtainable. A large number (44 per cent) of their cases were excluded because of lack of information. Since mothers are, in general, the most reliable source of anamnestic information, it is hardly surprising that the percentage of maternal deaths reported in their series of 200 schizophrenic patients was lower than expectation; in the 44 per cent of cases which were excluded because of lack of information, the percentage of maternal deaths would probably be considerably higher. From the standpoint of parental deaths, their series is, therefore, scarcely representative, and the small percentage of maternal deaths (which was presented as an incidental finding) would hardly be comparable to figures presented in other studies.

Since there was evidence that a disproportionately large number of patients with mental disease experience the death of their mothers during childhood, it seemed desirable to determine whether there was any critical age at which maternal bereavement would be more serious as a contributory or predisposing element in subsequent development of a psychosis. While statements have appeared in the literature,[6] based largely on individual case studies, stressing the importance of age at the time of bereavement, statistical studies on this topic have been infrequent. In fact, studies of maladjustment in the armed forces reveal a notable lack of agreement as to the age before which maternal death might be detrimental. Age limits selected by various authors include 18 years (Guttmacher and Stewart [7]), 17 years (Gardner and Goldman [8]), 16 years (Gardner and Aaron [9]) and 15 years (McNeel and Dancer [10]). Other age limits which appear in the recent literature are 12 years (Ruesch and associates [11]) and 6 years (Gardner and Aaron [9]). There is thus a wide discrepancy in the ages considered significant by the authors cited. If parental death, however, is actually more serious

5. Rosenzweig, S., and Bray, D.: Sibling Deaths in the Anamneses of Schizophrenic Patients, Arch. Neurol. & Psychiat. **49**:71 (Jan.) 1943.

6. English, O. S., and Pearson, G. H. J.: Common Neuroses of Children and Adults, New York, W. W. Norton and Company, Inc., 1937, p. 55.

7. Guttmacher, M. S., and Stewart, F. A.: A Psychiatric Study of Absence Without Leave, Am. J. Psychiat. **102**:74, 1945.

8. Gardner, G. E., and Goldman, N.: Childhood and Adolescent Adjustment of Naval Successes and Failures, Am. J. Orthopsychiat. **15**:584, 1945.

9. Gardner, G. E., and Aaron, S.: The Childhood and Adolescent Adjustment of Negro Psychiatric Casualties, Am. J. Orthopsychiat. **16**:481, 1946.

10. McNeel, R. H., and Dancer, T. E.: The Personality of the Successful Soldier, Am. J. Psychiat. **102**:337, 1945.

11. Ruesch, J.; Christiansen, C.; Pattern, L. C.; Dewees, S., and Jacobson, A.: Psychological Invalidism in Thyroidectomized Patients, Psychosom. Med. **60**:77, 1947.

at any age or ages, this fact should be susceptible of statistical demonstration. The study which indicated that maternal deaths might be related to subsequent development of psychosis, previously cited,[1] was based on 549 cases; in order to subdivide maternal deaths according to the age of the patient at the time of bereavement, it seemed desirable to enlarge the series to about three times this number.

METHODS AND DATA

The method employed was similar to that described elsewhere.[12] The material included the series previously reported, together with 683

TABLE 1.—*Incidence of Separation from Parents During Early Life of 852 Male and 831 Female Psychotic Patients by Death of Either Parent*

Age of Patient at Separation	Maternal Death			Paternal Death		
	Females	Males	Total	Females	Males	Total
0	7	4	11	7	2	9
1	5	8	13	2	9	11
2	6	7	13	6	5	11
3	8	8	16	5	3	8
4	7	4	11	12	5	17
5	10	9	19	5	8	13
6	12	8	20	7	6	13
7	8	7	15	6	7	13
8	7	4	11	6	5	11
9	6	6	12	9	9	18
10	4	7	11	10	6	16
11	8	1	9	10	5	15
12	4	8	12	10	5	15
13	5	3	8	12	12	24
14	11	4	15	7	7	14
15	11	6	17	16	4	20
16	12	5	17	14	12	26
17	5	7	12	6	11	17
18	5	8	13	9	13	22
19	10	6	16	9	14	23

additional patients, also from the New Jersey State Hospital, Greystone Park.[13] The latter, all representing first admissions, were under 40 years of age and entered this hospital from 1939 to 1945 inclusive. The anamneses of these 1,683 state hospital patients were inspected to determine whether either of the parents had died and the age of the patient at the time.

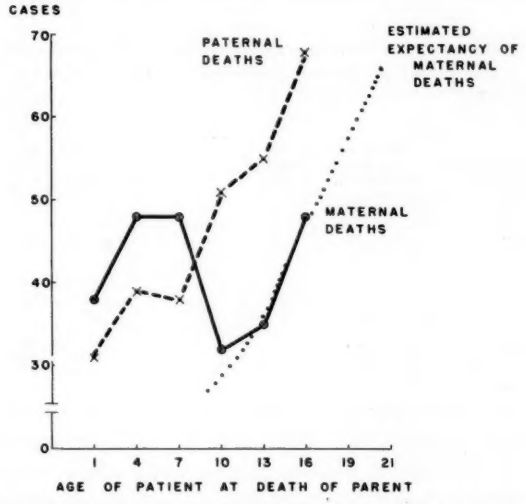
Table 1 shows the incidence of parental bereavement for this series for each year from the patient's birth to the age of 20. If the frequency of paternal deaths is analyzed according to the age of the patient at the time of bereavement, two trends appear: 1. A tendency toward a

12. Barry, H., Jr.: Incidence of Advanced Maternal Age in Mothers of One Thousand State Hospital Patients, Arch. Neurol. & Psychiat. **54**:186 (Sept.) 1945.

13. Case histories were made available through the courtesy of Dr. Marcus A. Curry.

secular rise in frequency of paternal death with increasing age of the patients. This is in accordance with statistical expectation, since mortality rates become greater with increasing age. 2. Variations from year to year. These are probably chance fluctuations. Final determination of whether yearly fluctuations are meaningful or are due to chance would require a large number of additional cases.

In contrast to the distribution of patients' ages at the time of paternal death, the ages of psychotic patients when their mothers died follow a different pattern. Three trends appear: (1) a relatively high rate of maternal bereavement during infancy and early childhood; (2) a marked decline in the incidence of maternal death during early adolescence; (3) an irregular, but definite, rise in the number of maternal



Maternal death rates for psychotic patients compared with parental death rates and estimated maternal death rates based on tables from Lotka.[20]

deaths from adolesence onward. This is roughly parallel to the rise in paternal deaths at the same ages and presumably has a similar explanation, in terms of greater mortality rates with increasing age.

In the chart, the results are presented graphically. In order to minimize purely incidental variations and to bring out the underlying trends, abscissas are based on three year intervals. It is evident that a disproportionately large number of maternal deaths occurred prior to the time that the patients were 8 years of age; during this period 7.6 per cent of the female patients and 6.4 per cent of the male patients had experienced the death of their mothers. In absolute terms this number is not large; only 1 of 14 female patients and only 1 of 16 male patients had experienced the death of their mothers by the age of 7 years. However,

the distribution of parental deaths suggests that the first seven years are critical so far as the presence of the mother is concerned. There is no evidence of a similar trend with respect to the patients' fathers.

Since maternal bereavement seems to be a sensitizing factor in the development of subsequent psychosis if it occurs prior to the age of 8, the question arises whether separation from the mother due to causes other than death might not also have a more traumatic effect if it occurred in early childhood. In a psychotic population, one obvious cause of a disrupted home during the patient's childhood might be the occurrence of a psychosis in either of his parents. While a great deal has been written about the hereditary aspects of mental disease, relatively little emphasis has been placed on the possible trauma to a child in having a parent in an institution for mental disease. For this reason, the ages of

TABLE 2.—*Incidence of Separation from Either Parent Due to Parental Commitment or Desertion for 1,683 Psychotic Patients*

Patient's Age at Separation	Maternal			Paternal		
	Commitment at Mental Hospital	Desertion, Etc.	Total	Commitment at Hospital	Desertion, Etc.	Total
Prior to birth of patient	4	..	..	1	..	..
0-3	10	8	18	5	10	15
4-7	9	6	15	10	7	17
8-11	8	1	9	7	9	16
12-15	5	2	7	10	4	14
16-19	7	5	12	3	4	7
Over 20	12	..	..	5	..	..
Total	55	..	..	41	..	..

patients at the times their parents were committed have been tabulated. It should be emphasized that these data do not represent all cases of mental illness in a parent, but are limited to cases in which the parent was committed to a psychiatric hospital and in which the age of the patient at the time of the commitment was available. The results are presented in table 2. While the absolute number of cases, when split into four year intervals, is too small to furnish any reliable conclusions, it will be seen that more mothers than fathers were committed during the first eight years of the patients' lives. During the next eight years, the opposite is true, more fathers than mothers being committed between the time that the patients were 8 and 15 years of age. Though these results are at best only suggestive, and obviously require confirmation with a larger series of cases, they are not inconsistent with the results obtained for parental deaths. The evidence at hand, therefore, suggests that the critical period for separation from the mother is before the age of 8, both when caused by death and when resulting from commitment to a psychiatric institution.

In the same table, figures are presented which show the age of the patient when a parent deserted, or when the patient had been otherwise separated from his parents. Again, there is a trend toward relatively more cases among patients who were separated from their mothers before they were 8 years of age. Although the absolute number of cases, again, is not large, the data indicate that separation from the mother occurred among psychotic patients more frequently before the patient was 8 years of age than after that time, whether this separation was due to maternal death, commitment to an institution, divorce or desertion.

In order to determine the age distribution of maternal deaths among psychoneurotic patients, it would be necessary to obtain a similar series of psychoneurotic case histories. These should, to be reliable, include

TABLE 3.—*Number of Psychoneurotic Patients Who Experienced the Death of Their Mothers Prior to 16 Years of age*

Age of Patient at Death of Mother, Yr.	Patient Group			
	Ward (Massachusetts General Hospital)	Private Practice	Riggs Foundation	Total
0-3	2	7	4	13
4-7	3	4	1	8
8-11	1	2	1	4
12-15	2	1	0	3
Total cases	118	109	103	330
Patients bereaved before age of 8				
Number	..	..	..	21
Percentage	..	..	..	6.4%

at least 1,500 cases. However, some clue to the actual distribution may be afforded by a smaller number. Data are therefore presented for 330 cases. These represent three social and economic groups, as represented by (*a*) 118 cases from the wards of Massachusetts General Hospital, (*b*) 109 cases from private practice in which a diagnosis of psychoneurosis was made and (*c*) 103 cases from the Austen Riggs Foundation, Stockbridge, Mass. The incidence of maternal deaths is presented in table 3.

It will be seen that 6.4 per cent of the psychoneurotic patients for whom data are available experienced the death of their mothers before they were 8 years of age. While the findings must be regarded as tentative, they suggest that maternal bereavement before the age of 8 years may also be related to later development of a psychoneurosis.

COMMENT

In recent discussion of psychiatric conditions, there has been an increasing tendency to accept multiple factors as playing a possible role in

the causation of mental illness.[14] While various proposals have been made for classifying the causes of psychiatric illness, there would appear to be some advantage in subdividing possible causal factors according to the period in the life history of the patient at which they became operative. The life chart as described by Muncie [15] and developed by Cobb [16] has proved a useful technic in showing the relation between events in a patient's life and the subsequent development of symptoms. In the life chart there are indicated several periods which may assume special significance. These include, first, a prenatal period: Prior to birth many elements may influence the developing organism, such as intrauterine infections, which may result in blindness or other malformations,[17] endocrine imbalance of the pregnant mother, which may adversely affect the developing fetus,[18] and other forces, characterized by Myerson [19] as blastophoria.

Second, after birth, and before the appearance of mental illness, there is usually a period of at least fifteen years. The patient who later becomes mentally ill may often be subjected to numerous traumatic situations during this interval. It has been difficult to determine whether these events actually play a part in the causation of psychiatric illness, because of the long period of latency which may elapse between the time of trauma and the actual onset of a psychosis later.

The ideal method of determining whether any factor contributes to the development of a psychosis might seem to involve a comparison of its relative frequency among psychotic patients and normal controls. Unfortunately, it is almost impossible to set up a strictly comparable control group for the study of parental deaths in a hospital population of this size because death rates vary widely according to social and economic status, national origin, date of birth, occupation and many other factors. However, a comparison of maternal and paternal death rates obviates this difficulty, especially since such comparisons have previously been made by Lotka [20] for large groups of normal persons. The results of such a comparison in a series of psychotic patients reveal a striking

14. Strecker, E. A., and Ebaugh, F. G.: Practical Clinical Psychiatry, ed. 5, Philadelphia, The Blakiston Company, 1940.

15. Muncie, W.: Psychobiology and Psychiatry, St. Louis, C. V. Mosby Company, 1939, p. 38.

16. Cobb, S.: Borderlands of Psychiatry, Cambridge, Mass., Harvard University Press, 1943, p. 8.

17. Wesselhoeft, C.: Rubella, New England J. Med. **236**:978, 1947.

18. Benda, C. E.: Mongolism and Cretinism New York, Grune & Stratton, Inc., 1946.

19. Myerson, A.: Inheritance of Mental Diseases, Baltimore, Williams & Wilkins Company, 1925, p. 286.

20. Lotka, A. J.: Orphanhood in Relation to Demographic Factors, Metron **9**:1-109, 1931.

preponderance of maternal over paternal deaths prior to the age of 8, followed by reversal to the normal preponderance of paternal deaths after this age. There is a similar tendency for maternal separation, due to hospitalization, etc., to occur more frequently during early childhood than when the patient is older.

A third, and final, period of importance in the life history of psychotic patients is the period immediately prior to the onset of symptoms. Events which occur at this time may be said to precipitate the illness. A study of parental deaths from this point of view is now in preparation.

The question whether the findings presented in this paper are consistent with psychoanalytic theory is not easy to answer. English and Pearson [6] stated that paternal loss is serious, but this does not seem to be true with the psychotic subjects in the present investigation. English and Pearson also stated that death is especially important if it occurs "during the height of the oedipus situation, i. e., four to seven years of age." The present findings are somewhat ambiguous in this connection because, though there is a tendency toward an increase in maternal deaths in the histories of psychiatric patients between the ages of 4 and 7 years, the increase is not much greater than that which might be anticipated because of increase in age of the mothers at this time. A comparison of maternal deaths among male and female patients does not show any notable differences beyond those which might result from chance variation. On the whole, it would seem to be most likely that the death of the mother may expose a very young child to neglect, hostile step-parents and other adverse influences. Final judgment on this topic may be deferred until the subsequent histories of patients who experience the death of their mothers during childhood have received further analysis.

CONCLUSIONS

1. Maternal deaths occurred in the histories of psychotic patients with increased frequency before the patients were 8 years of age.

2. Separation of psychotic patients from their mothers due to commitment of the mother to a psychiatic institution, to desertion or to the patient's being placed in a home tended to occur with increased frequency before the patients were 8 years of age.

3. There was no clear evidence that separation of patients from their fathers occurred with special frequency at any specific age.

4. Preliminary figures for psychoneurotic patients suggest that maternal bereavement before the age of 8 may be a sensitizing factor in the development of subsequent psychoneurosis.

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HERPES ZOSTER OF THE SEVENTH, EIGHTH, NINTH AND TENTH CRANIAL NERVES

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HERPES zoster affecting the head, especially auricular herpes zoster (herpes zoster oticus), is often associated with facial paralysis and lesions of the eighth nerve. Herpes zoster of the outer ear, combined with lesions of the seventh or the eighth cranial nerve or both, is generally called Hunt's syndrome. Hunt [1] discussed this syndrome in a series of papers. In connection with these studies, he suggested that the geniculate ganglion might be the origin of sensory fibers in the facial nerve, a theory which has received anatomic support. According to Hunt, the "geniculate area" would comprise the concha and certain other parts of the auricle, part of the external auditory meatus and some "remnants of the geniculate visceral sensory system" on the palate and tongue. Herpetic infection of the geniculate ganglion would produce vesicles in exactly this area. Although there is still no definite histopathologic evidence of the existence of herpetic lesions of the geniculate ganglion in cases of herpes zoster oticus, it has been generally accepted that this type of herpes zoster is caused by microscopic lesions affecting the geniculate ganglion.

The facial palsy and the lesions of the eighth nerve often associated with herpes zoster oticus are easily explained by assuming an increased pressure of the swollen geniculate ganglion on the facial nerve or extension of the infection to the facial or the auditory nerve. Simultaneous infection of the ganglia of the inner ear has also been suggested.

Facial paralysis and lesions of the eighth nerve associated with herpes zoster in the trigeminal or the cervical areas of the head, how-

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1. Hunt, R.: (*c*) Herpetic Inflammation of the Geniculate Ganglion: A New Syndrome and Its Complications, J. Nerv. & Ment. Dis. **34**:73, 1907; (*b*) The Sensory System of the Facial Nerve and Its Symptomatology, ibid. **36**:321, 1909; (*c*) The Symptom-Complex of Acute Posterior Poliomyelitis of the Geniculate, Auditory, Glossopharyngeal and Pneumogastric Ganglia, Arch. Int. Med. **5**:631 (June) 1910; (*d*) The Sensory Field of the Facial Nerve, Brain **38**:418, 1915; (*e*) Geniculate Neuralgia, Arch. Neurol. & Psychiat. **37**:253, 1937.

ever are more difficult to explain. According to Hunt, who included these types of herpes in his syndrome, the trigeminal or the cervical ganglion represented the main focus of infection, a hypothesis explaining the cutaneous manifestations. In addition, he postulated microscopic changes even in the geniculate ganglion which might entail pressure on the facial nerve or spread to the eighth nerve.

In 1910 Hunt [1c] pointed out that even herpetic lesions of the ganglia of the glossopharyngeal and vagus nerves might be responsible for herpes zoster oticus in some cases, since it is well known that the nerves in question innervate a small zone of the auricle via Arnold's nerve (ramus auricularis nervi vagi).

Herpes zoster of the glossopharyngeal and vagal territories is rare. Wilson [2] mentioned that little is known of herpes zoster of this localization. In the surveys of herpes zoster in the ordinary textbooks, herpetic involvement of the ninth and tenth nerves is usually not mentioned. However, descriptions of such cases are to be found in the literature. Hunt [1c] cited several earlier authors who had reported herpes pharyngis and herpes laryngis. Some of these descriptions seemed to relate to cases of true herpes zoster with unilateral distribution of the vesicles, while many authors discussed other types of herpetic eruptions.

Glossopharyngeal or vagal herpes zoster with eruptions even in the auricle have been reported in a few instances (Hall,[3] Chauveau,[4] Désirat,[5] Worms and Lieux,[6] Baldenweck and Degorce,[7] Watson,[8] Negus and Crabtree [9]).

In Hall's case there were also vomiting and hiccups (signs of vagal involvement) and in the case of Worms and Lieux palatal and laryngeal paralysis was present. In the case of Negus and Crabtree there were facial palsy and pharyngeal and laryngeal paralysis.

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2. Wilson, S. A. K.: Neurology, edited by A. Ninian Bruce, Baltimore, William Wood & Company, 1940.

3. Hall, J. N.: Herpes of Mucous Membrane and Skin, Brit. M. J. **1**:848, 1897.

4. Chauveau: Herpès du tympan avec un herpès guttural et labial, Ann. d. mal. de l'oreille **27**:151, 1901.

5. Désirat, A. J.: Complications à l'étude de quelques complications rares du zona ophtalmique, Thèse de Bordeaux, 1903, p. 20.

6. Worms, G., and Lieux, P.: Zona otitique associé à des paralysies faciale et palato-laryngée, Rev. d'oto-neuro-ocul. **4**:306, 1926.

7. Baldenweck and Degorce: Zona otique total, associé a un zona du trijumeau, du glosso-pharyngien et du laryngé supérieur, Rev. d'oto-neuro-opht. **17**: 29, 1939.

8. Watson, H. A.: Herpes Zoster Oticus with Involvement of Seventh, Eighth, Ninth and Tenth Nerves and with Possible Involvement of Second Division of Fifth Nerve, M. J. Australia **2**:171, 1941.

9. Negus, V. E., and Crabtree, N. C.: A Case of Herpes Zoster of the Seventh, Ninth and Tenth Cranial Nerves, J. Laryng. & Otol. **58**:192, 1943.

Prior to Hunt, cases of herpes zoster oticus associated with lesions of the seventh and eighth nerves or both had been reported by several authors (Gruber,[10] 1887; Politzer,[11] 1893; Hammerschlag,[12] 1899; Körner,[13] 1904). The literature on Hunt's syndrome has been reviewed by several authors when reporting cases of their own (Haymann,[14] Hill,[15] O'Neill,[16] Tschiassny [17]).

Von Frankl-Hochwart [18] (1905) proposed the term "polyneuritis cerebralis ménièriformis" for the acute vestibular irritation combined with deafness and facial palsy. Antoni [19] (1919) pointed out that apparently this syndrome is often identical with the syndrome of Ramsay Hunt, since in many cases of this type herpetic vesicles have been found in the auricle and the external auditory canal. Key-Åberg [20] agreed with Antoni in this respect.

It is surprising that the possibility of changes in the ganglia of the ninth and tenth nerves has seldom been discussed in the many cases of herpes zoster oticus which have been reported during the last decades. O'Neill,[16] on criticizing Hunt's concept of changes in the geniculate ganglion as a cause of herpes zoster oticus, emphasized that "unquestionably in many cases of aural herpes fulminating vagal symptoms are mistaken as vestibular."

During the last year we have observed 4 cases which may be of interest in a discussion of the origin and complications of herpes zoster oticus. In 2 cases herpetic eruptions were present in the territories of the ninth and tenth nerves in the pharynx and larynx, with motor complications referable to the same areas. In both cases vesicles were found also in the "Hunt area" of the outer ear and the mouth, and in both the

10. Gruber (1887); cited by Key-Åberg.[20]

11. Politzer, cited by Hammerschlag.[12]

12. Hammerschlag: Beitrag zur Casuistik der multiplen Hirnnervenerkrankungen, Arch. f. Ohrenh. **45**:1, 1898.

13. Körner, O.: Ueber den Herpes zoster oticus, München. med. Wchnschr. **51**:6, 1904.

14. Haymann, L.: Ueber Zostererkrankungen im Ohrgebiet, Ztschr. f. Hals-, Nasen- u. Ohrenh. **1**:397, 1922.

15. Hill, F. T.: Herpes Zoster Oticus: Report of Three Cases, Ann. Otol., Rhin. & Laryng. **45**:666, 1936.

16. O'Neill, H.: Herpes Zoster Auris ("Geniculate" Ganglionitis): Report of Eight Cases with Photographs of So-Called Syndrome of Ramsay Hunt, Arch. Otolaryng. **42**:309 (Nov.-Dec.) 1945.

17. Tschiassny, K.: The Site of the Facial Nerve Lesion in Cases of Ramsay Hunt's Syndrome, Ann. Otol., Rhin. & Laryng. **55**:152, 1946.

18. von Frankl-Hochwart, L.: Erfahrungen über Diagnose und Prognose des Ménièreschen Symptomenkomplexes, Jahrb. f. Psychiat. u. Neurol. **25**:245, 1905.

19. Antoni, N.: Herpes zoster med förlamning, Nord. med. (hygiea) **81**:340, 1919.

20. Key-Åberg, H.: Herpes zoster oticus, Acta oto-laryngol. **10**:209, 1927.

eighth nerve was involved. In the third case Hunt's syndrome was associated with herpes zoster oticus, vesicles in the mouth, facial paralysis with hypogeusia and symptoms referable to the eighth nerve. The patient, however, also had unilateral laryngeal and pharyngeal paralysis.

In the fourth case, finally, there was eruption in the areas of the ninth and tenth nerves, including the ear. Furthermore, there were motor complications associated with lesions of the seventh, ninth and tenth nerves, as well as cochlear and vestibular symptoms.

REPORT OF CASES

CASE 1.—A farmer, aged 64, was said to have had pneumonia thirteen times. On all occasions he had been treated at home, and roentgenographic examination was never performed. At the age of 61 he was hurt by a cow and sustained a lesion of the upper left brachial plexus. For many years he had had slowly progressive bilateral deafness. During the last half-year he had been in rather good health and had been working as usual.

On Jan. 16, 1947, at the age of 64, he had a headache, which increased during the following days. On January 19 he felt pain in the left side of the neck, sometimes radiating into the left arm. About the same time he experienced pain in his left ear and dizziness. He also complained of sore throat, but all the symptoms were on the left side. On January 20, he observed small vesicles in the concha of the left ear and a small group of vesicles below the left ear. About this time hoarseness was also noticed; the deafness increased on the left side, and he had difficulty in swallowing. He also felt pain in the left side of the chest and in the left posterior part of the tongue.

He was then seen by a physician and was admitted to the hospital with a diagnosis of peritonsillar abscess (angina tonsillaris), otitis of the middle ear and accessory sinuses, vertigo and tenderness over the mastoid process.

On admission (January 21) he was in a rather serious condition. He was grayish pale and displayed an obvious tendency to fall backward and a little to the left. He had nystagmus of the lateral-rotary type to the right and of the first degree, not changing with the position.

There was no facial palsy, and no difference in taste sensation between the right and the left half of the tongue could be established.

Ears.—Right Ear: The drum membrane was slightly thickened. The external ear was normal.

Left Ear: About 2 cm. below the external ear was a patch of herpetic lesions of typical zoster character (fig. 1). On the pinna and in the posterior part of the external meatus were several vesicles with clear, watery contents. Some of these vesicles had ruptured, so that there was an appearance of a slight discharge from the ear. The drum membrane had a small, dry perforation. Conversation was heard at about 1 meter. In the Weber test sound was lateralized to the right. The Rinne test was positive, and Schwabach's test showed shortening of bone conduction.

Mouth and Pharynx.—The mouth and pharynx were fairly normal on the right. On the left side of the tonsillar region and the posterior third of the tongue and along the middle part of the left margin of the tongue, as well as on the posterior wall of the pharynx were a great number of yellowish white patches with livid, reddened surroundings, and in some places actual vesicles (fig. 2). Changes of similar nature were seen also in the left vallecula epiglottica, the left half of

the epiglottis, the left piriform sinus, the false and real vocal cords on the left and a space of at least 3 to 4 cm. in the subglottic area. The efflorescenses were distinctly localized to the left side, with a sharp border toward the normal right half of the pharynx. No changes were seen in the nasopharynx.

The motility of the larynx and piriform sinus seemed to be normal on the right side, whereas it was absent on the left side, with no perceptible movements of the vocal cord. There was a *signe de rideau* to the right.

Fig. 1 (case 1).—Herpes zoster lesions on the pinna and over the neck below the ear.

Fig. 2 (case 1).—Lesions of herpes zoster on the left side of the pharynx. Facial motility was normal.

Caloric Reaction.—On his admission there was a depressed reaction on the left side. Several days after admission no reaction could be elicited on this side with great amounts of cold water.

Lumbar Puncture (January 24).—The initial pressure was 95 mm., with 19 red cells and 268 white cells (10 per cent polymorphonuclear cells and 90 per cent mononuclear cells) per cubic millimeter. The sugar content was 73.

Course of Illness.—Except for the signs mentioned and the lesions of the left brachial plexus, the neurologic findings were normal.

The patient had great difficulty in swallowing. Food and fluid passed into the lungs, and symptoms of bronchopneumonia developed. On some occasions the pulse rate was irregular, that is, sometimes slow and sometimes quickened. He had precordial pain. Electrocardiograms taken on two occasions were normal, but the pulse was normal at that time.

It was necessary to feed the patient through a tube inserted through the right nasal cavity and on the right side of the pharynx. An attempt to insert the tube on the left side entailed severe pain.

The temperature was about 38 C. (100.4 F.) during the first fourteen days of hospitalization, with some increases to about 39 C. (102.2 F.) when symptoms of pneumonia occurred. After fourteen days the temperature dropped gradually. The patient slowly learned to feed himself but was obliged to take small pieces of food each time, and he could drink only a little at one time.

The paralysis of the larynx and pharynx showed no signs of clearing, and the left vocal cord was immobile, in the cadaveric position, when he was last seen, about two months after admission. The patient had at that time pronounced loss of hearing, which showed no signs of improving.

CASE 2.—The patient, a woman aged 68, had a sister who several years before had been treated for herpes zoster ophthalmicus. The patient herself had usually been in good health. She was suddenly taken ill on Aug. 30, 1947, with intermittent fever (temperatures up to 39 C.); pain in the left ear, the left side of the neck and along the left margin of the tongue, and lesions of the skin and mucous membrane of almost the same distribution as that in case 1 (fig. 3). In the larynx, however, the herpetic eruptions affected only the ventricular surface, and not the vocal cords. The left vocal cord was slightly paretic. In the nasal portion of the pharynx, lesions were noted only in the lowest parts. The hearing, which earlier had been quite normal, was slightly reduced, and an audiogram showed reduction of perception particularly for high tones. There were no vestibular symptoms. The spinal fluid showed pleocytosis, that is, 102 cells per cubic millimeter (95 mononuclear cells and 7 polymorphonuclear leukocytes) and a slight increase in proteins. There was no facial paralysis or disturbance of taste. The pulse rate and the electrocardiogram were normal. There was no difficulty in swallowing. After about fourteen days the patient had practically recovered. The lesions had disappeared; there were no palsies, and hearing was practically restored.

CASE 3.—A man, aged 52, an engineer, during the past few years had had mild cardiac symptoms. About Oct. 20, 1947 he was suddenly taken ill with severe pain in the left side of the face, the left side of the neck and around the left ear. He was treated by a physician with sulfadiazine. Toward the end of October a few herpetiform lesions developed on the trunk and the lower extremities, as well as groups of similar vesicles in the external auditory meatus, the left tonsillar region and along the left lateral margin of the tongue (fig. 3). About November 1 the patient presented palsy of the left side of the face of peripheral type and experienced hoarseness and difficulty in swallowing. His hearing, which had previously been slightly impaired on both sides, was at that time very much reduced on the left side, so that he scarcely heard conversation. He had vertigo and a marked tendency to fall to the left. The caloric reaction was weak on both sides. There was hypogeusia of the left half of the tongue. The electrocardiogram was normal. The spinal fluid showed a mononuclear pleocytosis (94 cells per cubic millimeter, 92 of which were mononuclear and 2 polymorphonuclear cells) and a slight increase in proteins.

He had a lateral-rotary nystagmus to the right of the first degree. There were *signe de rideau* to the right and slight paralysis of the left side of the palate. He had severe difficulty in swallowing, and during the first part of his stay in the hospital he was fed through a tube. On his admission, the left half of the larynx was immobile, as well as the piriform sinus.

The facial paralysis showed satisfactory regression in about two weeks, but the laryngeal paresis did not improve until about six weeks after the onset of hoarseness. There was then good regression, and when the patient was last seen the larynx showed only a slight reduction in movement on the left side.

This case was one of herpes zoster oticus with facial paralysis and slight neuritis of the left acoustic nerve—a case of Hunt's syndrome combined with paralysis of the left vagus nerve.

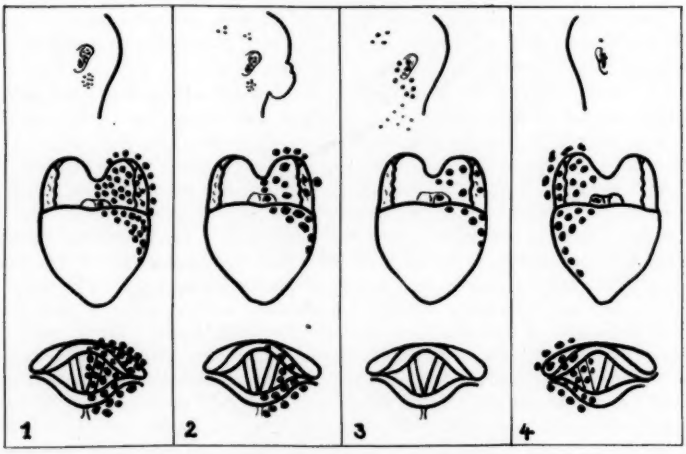

Fig. 3.—Schematic drawings showing the distribution of the herpes zoster vesicles in cases 1, 2, 3 and 4.

CASE 4.—A man aged 57, a workman, was said to have had pneumonia five times during the period from 1912 to 1934.

On May 31, 1948 he felt ill and experienced pains in the right side of his throat. The pains became progressively worse until June 2, when he also felt pain in his right ear. At the same time he had difficulty in swallowing and hoarseness. On June 4 herpetic eruptions appeared on the right ear and in the auditory canal and were also observed in the right tonsillar and palatal region. About the same day deafness appeared on the right side, but there was no dizziness.

On his admission (June 8) the general condition was moderately affected. There were herpetic eruptions in the right auditory canal, especially the posterior part, but small vesicles were also found anteriorly. Eruptions were also observed on the pinna of the right external ear, on the right margin of the tongue, on the right plica glossoepiglottica and in the tonsillar region. The herpetic vesicles and membranes also appeared on the right half of the epiglottis and in the pharynx

(except the upper part of the epipharynx) and could be seen on the right false vocal cord, the vallecula epiglottica and the piriform sinus (figs. 3 and 4). There was palatal and pharyngeal paralysis on the right side, and the ventricular area and vocal cords did not move as well on the right as on the left.

Hearing was moderately reduced, and an audiogram showed reduction of perception for high tones. There were no vestibular symptoms. General somatic and neurologic examinations revealed nothing of interest. The electrocardiogram was normal.

On June 9 the patient complained of dizziness, and on June 10 he had pronounced vertigo with lateral-rotary nystagmus of the second degree to the

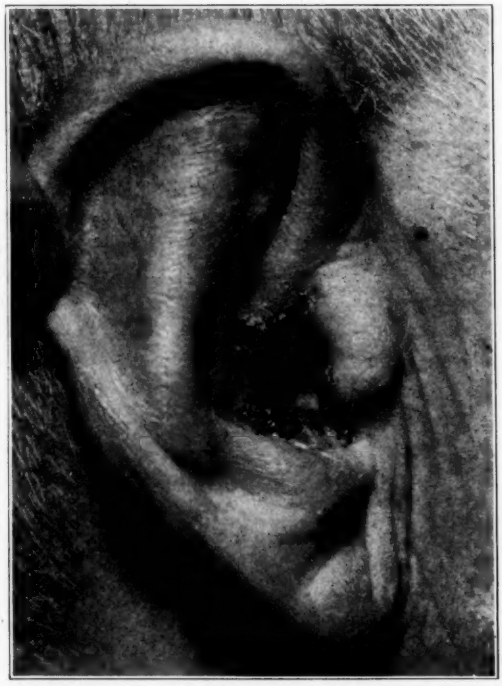

Fig. 4 (case 4).—An eruption of herpes zoster in the aural concha. The distribution was at the beginning of somewhat greater extent.

left, not changing with the position. He had a tendency to fall to the right. The herpetic eruptions were still visible.

Examination of the lumbar fluid on June 10 showed an initial pressure of 180 mm. of water and a white cell count of 83 (7 polymorphonuclear and 76 mononuclear cells) per cubic millimeter. The protein content was slightly increased.

Two days later (June 12) facial paralysis of peripheral type appeared on the right side. The herpetic eruptions had now almost completely disappeared. The swallowing was much better, but there was still slight laryngeal paralysis on the right. There was no hypogeusia. Lacrimation, produced by chemical

stimuli, was reduced on the right. Three weeks later the facial paralysis was unchanged, but the pharyngeal and laryngeal paralysis had disappeared. The hearing faculty of the right ear was much better.

COMMENT

Since Cushing's [21] classic publication (1904) on the sensory distribution of the trigeminal nerve, it may be regarded as an established fact that the trigeminal area extends backward to the anterior part of the auricle and the anterior wall of the external auditory meatus, and probably often to the anterior part of the tympanic membrane. It is also generally accepted among both anatomists and clinicians that the posterior part of the auricle belongs to the cervical sensory area. Between the trigeminal and the cervical area of the auricle there is, however, interposed an area (concha auriculi, antitragus, part of the tragus, part of the anthelix, part of the fossa anthelicis, posterior part of the external auditory meatus, the posterior part of the tympanic membrane) which is innervated neither by the trigeminal nerve nor by the cervical nerves. The parts mentioned are the destination of the auricular ramus of the vagus nerve, which also innervates a small area at the dorsomedial surface of the auricle. Many authors are of the opinion that the glossopharyngeal nerve also takes part in the innervation of this field by communications with the vagus nerve.

Hunt,[1] in a series of papers, discussed the possibility of a field of cutaneous sensory innervation belonging to the intermediofacial nerve (pars intermediafacialis). This field would also be interposed between the trigeminal and the cervical area of the auricle and would consequently correspond chiefly to the vagal area. Hunt stated that, according to studies in comparative anatomy, cutaneous fibers are found in the seventh nerve of selachians, teleosts and amphibians and that theoretically there can be no objection supposing that the intermediofacial nerve, as belonging to the second branchial arch, has a somatic sensory area even in man. He drew attention to the fact that herpes zoster oticus is often combined with facial paralysis and proposed the hypothesis that the inflammatory process may in such cases be localized to the geniculate ganglion. He maintained that the localization of the vesicles in herpes zoster oticus, as well as of the pain, demonstrated the cutaneous and mucous distribution of fibers of the intermediate nerve.

Hunt based his opinion also on a case of "geniculate neuralgia" described by Clark and Taylor [22] (1909) in which cure was effected by intracranial discission of the intermediate nerve. The pain in that case

21. Cushing, H.: The Sensory Distribution of the Fifth Cranial Nerve, Bull. Johns Hopkins Hosp. **15**:213, 1904.

22. Clark and Taylor (1909); cited by Hunt.[1c]

was typically neuralgic and was localized chiefly to the deep portion of the ear, to the anterior wall of the external auditory meatus and to a small area just in front of the ear.

Hunt's hypothesis of an area of sensory innervation of the intermediofacial nerve has been accepted by most authors and has received anatomic support. Thus, Rhinehart [23] and Larsell and Fenton [24] could in the mouse and in man demonstrate fibers from the intermediate nerve joining the auricular ramus of the vagus nerve and being then distributed to the skin of the auricle. Villiger and Ludwig,[25] however, stated that the theory of Hunt is unconvincing. Hunt's hypothesis has also been criticized by Mills,[26] O'Neill [16] and others.

The sensory innervation of the oral cavity, pharynx and larynx is much less disputed, though there is some overlapping of the areas of innervation of the cranial nerves concerned. Points of interest in connection with the cases described in this paper will be discussed later.

Cases 1 and 2 in our series were very similar. The vesicles were found in regions corresponding to the distribution of the vagus, and probably also the glossopharyngeal, nerve (fig. 3). The vesicles in the tonsillar region and the posterior part of the tongue were situated in areas which are said to be innervated by the glossopharyngeal nerve; so it does not seem possible to assume that lesions of the vagus nerve alone are responsible. Both the patients suffered from pain in the ear, the left side of the neck and along the left margin of the tongue. The first patient also complained of pain radiating into the left arm and the left side of the chest. This patient also had attacks of tachycardia. In both cases there were motor symptoms—in case 1 extensive paralysis of the left side of the pharynx and larynx and in case 2 a slight paralysis of the left side of the larynx. In both cases lesions of the eighth nerve were also presented—vestibular and cochlear in case 1 and cochlear only in case 2.

It must be considered established that the main herpetic lesions in the 2 cases were limited to the vagal and glossopharyngeal ganglia. As the eruption in the pharynx and larynx must be due to changes in the ganglia mentioned, there is little reason to discuss the possibility of lesions even in the geniculate ganglion, though vesicles occurred also

23. Rhinehart, D. A.: The Nervus Facialis of the Albino Mouse, J. Comp. Neurol. **30**:81, 1919.

24. Larsell, Õ., and Fenton, R. A.: The Embryology and Neurohistology of Sphenopalatine Ganglion Connections: A Contribution to the Study of Otalgia, Laryngoscope **38**:371, 1928.

25. Villiger, E., and Ludwig, E.: Die peripherale Innervation, Basel, Benno Schwabe, 1946.

26. Mills, C. K.: The Sensory Functions Attributed to the Seventh Nerve, J. Nerve. & Ment. Dis. **37**:353, 1910.

in the "Hunt area" of the ear and mouth. As already mentioned, this area, however, may even be innervated by the ninth and tenth nerves.

The pain radiating into the left arm in case 1 may perhaps be interpreted as produced by distant changes associated with the herpes zoster, localized to cervical roots. This assumption is not far fetched, since there was general slight meningitis in our cases and it is now well known that anatomic examination may sometimes reveal distant changes in the nervous system. Magnusson and Wohlfart,[27] on anatomic examination in a case of herpes zoster ophthalmicus, found slight general meningitis and herpetic changes in the gasserian ganglion on both sides, though they were most pronounced on the side of the vesicles.

In this connection, it should be emphasized that in severe forms of neuralgia after "geniculate" herpes zoster the pain is sometimes felt in the neck and shoulder of the affected side (Hunt [1e]). In case 1 pain was also reported in the left side of the chest. This pain may perhaps be explained by aspiration of food and fluid due to the pharyngeal paralysis; but, as it was on the left side only, it may have been the expression of a herpetic inflammation of the bronchi (Duperrat [28]).

The attacks of tachycardia in case 1 were probably caused by a lesion of the vagus nerve.

Case 3 was of a somewhat different type—it was a typical instance of Ramsay Hunt's syndrome with herpes zoster oticus, facial paralysis and lesions of the eighth nerve. Taste sensibility was affected on the left side. There was, however, also weakness of the left side of the palate, pharynx and larynx, indicating a lesion of the vagus (and glossopharyngeal ?) nerves.

If the Hunt syndrome is produced by lesions of the geniculate ganglion, the vagoglossopharyngeal signs might, of course, be explained by assuming herpetic lesions of the roots of the nerves in question. As herpes zoster is anatomically sometimes more widespread than is usually apparent from the clinical picture, this assumption is not fanciful. One could, however, equally well explain the picture as chiefly a herpetic involvement of the vagus nerve with distant changes in the facial and acoustic nerves. The corresponding distribution of the vesicles in the outer ear, tongue and palate in our 4 cases (fig. 3) would thus obtain a common explanation.

Case 4, finally, may be regarded as a combination of the typical Hunt syndrome, with facial paralysis and cochlear and vestibular symptoms, and a vagoglossopharyngeal herpes zoster, with pharyngolaryngeal eruptions and paralysis. In our opinion, it must be regarded as

27. Magnusson, and Wohlfart, G.: Beitrag zur Klinik und Pathologie der Zostererkrankung, Deutsche Ztschr. f. Nervenh. **153**:225, 1942.

28. Duperrat, R. B.: Les manifestations viscérales du zona, Ann. de dermat. et syph. **5**:18, 1945.

most probable that the herpetic lesions in this case were mainly vagal and glossopharyngeal. There seems to be no reason to assume inflammatory lesions of the geniculate ganglion here.

The geniculate ganglion was studied, anatomically with autopsy in only 2 cases of Hunt's syndrome. Maybaum and Druss [29] observed changes in this ganglion in a case of periarteritis nodosa with herpes zoster oticus and facial paralysis. Denny-Brown, Adams and Fitzgerald [30] stated, however, that the histopathologic changes did not resemble those of herpes zoster.

Denny-Brown and his co-workers studied anatomically a case of herpes zoster of the occipital and collar region with facial paralysis and found pronounced changes in the second and slight changes in the third cervical ganglion, but a normal geniculate ganglion. Along the facial nerve they found areolar infiltration. Unfortunately, they omitted to examine the ganglia of the vagus and glossopharyngeal nerves. The investigations of Denny-Brown and his co-workers make it probable that herpes zoster of the occipital and collar region combined with facial paralysis is not regularly associated with changes in the geniculate ganglion, as was thought by Hunt. Probably the same statement may be made with respect to trigeminal herpes zoster combined with facial paralysis. On the other hand, the question whether herpes zoster oticus is due to lesions of the geniculate ganglia is still unanswered. This problem is easily applicable in many cases. At any rate, the hypothesis of Hunt is ingenious, but clarifying histopathologic investigations are still wanting.

Our cases indicate, however, that in the future it will be important in cases of herpes zoster oticus to make a careful clinical and, when there is an opportunity, a histologic investigation of the range of distribution of herpetic changes in the ninth and tenth cranial nerves. That the facial nerve, on the whole, seems to be vulnerable in herpes zoster of the head readily suggests that perhaps herpes zoster oticus may frequently be due to lesions of the glossopharyngeal and vagus nerves, supposed lesions of the seventh and eighth nerves being then interpreted as distant changes in the nerves in question. Since it is established that the facial nerve subserves sensory innervation of the concha, it is probable that changes in the geniculate ganglion may be the cause of certain cases of herpes zoster oticus. Tschiassny [17] concluded that the geniculate ganglion is involved in herpes zoster oticus with facial palsy, but not in cervical or trigeminal herpes zoster with facial palsy.

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29. Maybaum, J. L., and Druss, J. G.: Geniculate Ganglionitis (Hunt's Syndrome): Clinical Features and Histopathology, Arch. Otolaryng. **19**:574 (May) 1934.

30. Denny-Brown, D.; Adams, R. D., and Fitzgerald, P. J.: Pathologic Features of Herpes Zoster, Arch. Neurol. & Psychiat. **51**:216 (March) 1944.

In our 4 cases there were vesicles on the lateral margin of the anterior part of the tongue in a similar distribution. This observation may indicate that this area is actually innervated by the glossopharyngeal nerve.

Wakeley and Mulvaney,[31] in reporting 2 cases of Hunt's syndrome with a vesicular rash on the hard and soft palates and in the nose, mentioned that vesicles on the anterior two thirds of the tongue have been observed by only a few authors. They accepted Hunt's view that the occurrence of these vesicles in only a minor percentage of cases, even those with gustatory disturbances, must depend on the abnormal presence of ordinary sensory nerve fibers in the gustatory pathway (chorda tympani).

The frequency of vesicles and other signs in our 4 cases was somewhat variable. In case 1 the illness commenced with pain, after which within about one day there occurred vesicles and symptoms of functional impairment of the eighth and tenth nerves. In case 2 all the symptoms developed within one day, whereas in case 3 the first symptom was pain. Ten to eleven days later the vesicles first appeared, and the following day impairment in nervous function was noted. In case 4, finally, the disease started with pain. About two days later difficulty in swallowing and hoarseness appeared. On the fifth day herpetic eruptions and deafness were noted; on the eleventh day dizziness with nystagmus occurred, and on the thirteenth day the facial palsy started.

In this connection it should be pointed out that the vesicles in the mouth and pharynx are apt to remain as vesicles proper for only a short time; later they rupture and leave a necrotic area.

Hill [15] pointed out that all kinds of variations are common in the course of otic herpes zoster. Several authors have found that facial palsy may precede the eruption (Closier [32]; Haymann [14]; Lemaitre, Baudouin and Sailly [33]). This possibility is of importance in examination of facial paralysis immediately after their appearance. Especially if severe pain occurs with Bell's palsy, one should consider the possibility of herpes zoster oticus.

Differential Diagnosis.—Obviously, if only a superficial examination had been made in case 2, the condition might erroneously have been diagnosed as geniculate herpes zoster, since the signs of vagoglossopharyngeal injury would have escaped observation.

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31. Wakeley, C. P. G., and Mulvaney, J. H.: A Rare Feature of the Ramsay Hunt Syndrome, with Some Observations on the Sensory System of the Seventh Nerve, Lancet **1**:746, 1939.

32. Closier, L.: De l'herpes zoster auriculaire et para-auriculaire, Thèse de Paris, 1911.

33. Lemaitre, E.; Baudouin, E., and Sailly: Zona de l'oreille avec paralysie facial, Bull. et mém. soc. méd. d. hôp. de Paris **51**:503, 1927.

Herpes zoster oticus is generally regarded as a rare disease, an opinion which probably is incorrect. Rather, it is a disease that is rarely recognized. "The majority of the patients are seen by physicians in general practice, and the condition is constantly misdiagnosed as eczema, a stroke or Bell's palsy, and the rarity is more apparent than real." [16]

From an otologic point of view, cases of herpes zoster oticus are of great interest. When the factors of importance in laryngeal paralysis are studied, herpes zoster is seldom mentioned. It is probable that herpes zoster of the vagus nerve is a factor of importance, hitherto much neglected. In cases of laryngeal paralysis, the otologists and general practitioners must examine for possible zosteric eruptions and, if such are not found, they should question the patient in this respect. It is also important to make a careful study of cases with herpetic eruptions in the aural concha and external auditory meatus with regard to disturbances of hearing and equilibrium. It is probable that many conditions called external otitis will after a careful study prove to be zosteric in nature. This will explain the occasional association of herpetic lesions with vertigo and acoustic neuritis.

It is also of importance to consider herpes zoster oticus when discussing the cause of sudden loss of hearing. Herpes zoster oticus may occur with only a few, or with transient, vesicles in the aural region, whereas the loss of hearing may be of much greater importance.

Finally, it may be mentioned that our series comprised a case of bilateral herpes zoster oticus, which is not described here. In this case there were herpetic lesions in both aural conchas with practically total loss of hearing on the right side and moderate loss of hearing on the left side. Facial palsy did not occur in this case.

SUMMARY

Three cases of vagoglossopharyngeal herpes zoster with an eruption in the tonsillar region, on the palate and in the pharynx and larynx are reported. In all cases vesicles could be observed also in the auricle and the external auditory canal, corresponding to the area innervated by the ramus auricularis nervi vagi (Arnold's nerve). Signs referable to the acoustic and the motor portions of the vagus nerve occurred in all 3 cases, with facial paralysis in 1 case.

A case of Ramsay Hunt's syndrome (herpes zoster oticus, facial palsy and acoustic lesions) is described. In this case there was also paralysis of the left side of the pharynx and larynx, indicating injury to the vagus nerve.

It has not been definitely established that herpes zoster oticus in the Hunt syndrome is caused by changes in the geniculate ganglion. This is probable, however, since Hunt's theory pertaining to a sensory innervation of the outer ear and auditory canal by the pars intermedia

facialis has received anatomic support. Our cases, however, indicate that herpes zoster oticus may also be of vagoglossopharyngeal origin.

The lumbar fluid in our 4 cases showed a mononuclear pleocytosis, a finding which is commoner in all types of herpes zoster than is generally believed.

In the 4 cases reported vesicles of herpetic zoster were present along the anterior lateral margin of the tongue, indicating that this part of the tongue may be innervated by the glossopharyngeal nerve.

The term Ramsay Hunt's syndrome should be restricted to herpes zoster oticus with facial paralysis or lesions of the eighth nerve or both. "Occipital-collar" or trigeminal herpes zoster should not be included in the syndrome mentioned.

In cases of acute onset of facial paralysis, deafness, vertigo or laryngeal palsy, vesicles of herpes zoster should be looked for, especially in the auricle and the outer auditory canal. Herpes zoster oticus seems to be commoner than is usually thought, and in most cases it is probably misdiagnosed.

NOTE.—A fifth case with zoster eruptions in the aural concha, pharynx and pyriform sinus and on the tongue and with facial, pharyngeal and slight laryngeal paralysis has recently been observed by us. There were severe disturbances of audition and equilibrium.

Karolinska Institutet.

MEDULLOBLASTOMA

Report of a Case with Discussion of Origin

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THE CLINICAL course and the pathologic anatomy of the medulloblastoma have been repeatedly reported and clearly defined since the tumor was described to the American Neurological Association by Bailey and Cushing in 1924.[1] However, an interesting case of this tumor has directed my attention to the extensive study and conflicting nature of the theories dealing with its origin. The undifferentiated nature of the cells composing the neoplasm led the original authors to the belief that these cells, if of ectodermal origin, must be akin to the *indifferenten Zellen* of Schaper. Such cells had been previously identified (Pfleger) in heterotopic cellular groups in the region of the fourth ventricle, and Bailey and Cushing expressed the belief that "if such an isolated and retarded group of undifferentiated cells should undergo a neoplastic transformation, just such a tumor as we have described might be expected to result." [1] Although this theory is quite plausible, lack of indisputable evidence of this derivation and observations of other material has led to several counterproposals of origin. In support of the origin of medulloblastoma from cell rests near the fourth ventricle, the following case is reported.

REPORT OF CASE [2]

A 17 month old white girl entered the University of Arkansas clinic for the first time July 2, 1948, with the complaints of weakness of the neck and vomiting of four weeks' duration. About four weeks prior to admission the mother also noted that the child would hang her head and slept more than usual. She took the child to several physicians, one of whom noted a slight spasm of the right sternomastoid muscle without other symptoms and felt that the patient might have had a mild or early poliomyelitis. Shortly thereafter the child began to have early morning vomiting, and anorexia developed. She was examined again by her local

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Research paper no. 886 Journal series, University of Arkansas.

From the Department of Pathology, University of Arkansas School of Medicine and University Hospital.

1. Bailey, P., and Cushing, H.: Medulloblastoma Cerebelli: A Common Type of Midcerebellar Glioma of Childhood, Arch. Neurol. & Psychiat. **14**:192 (Aug.) 1925.

2. Dr. Anderson Nettleship helped in the preparation of this report.

physician on June 30, at which time she was stuporous. The pupils were reported as widely dilated but reacting to light, and she was said to have had a paresis of the left sternomastoid muscle rather than a stiff neck. On July 2, the local physician reported she had a rigid neck, right internal strabismus and nystagmus and had had convulsions of an indefinite nature which he had not witnessed. She was reported by her mother to have had a tremor of her hands at this time.

The child was apparently normal at birth and developed normally.

The temperature on admission was 105.6 F., the respiration rate 44 and the pulse rate 120. The patient was a well developed, well nourished white child, who was lethargic and completely unresponsive. Small crusted and indurated cutaneous lesions were noted on both buttocks. No deformity or tenderness of the skull was noted. The pupils were dilated and did not respond to light or in accommodation. Bilateral papilledema and large retinal veins were noted; there was left lid drop. The neck and back were definitely stiff. Coarse rhonchi were heard over both pulmonary fields. There were no abnormal cardiac or abdominal conditions observed. There were a positive Kernig reflex and an abnormal Babinski sign. The child had several spastic convulsions at the time of examination.

The laboratory examination on admission revealed an erythrocyte count of 5,900,000, with 18 Gm. of hemoglobin. The leukocyte count was 16,400, of which 1 per cent were stab cells, 70 per cent segmented cells, 27 per cent lymphocytes and 2 per cent mononuclear cells. A spinal puncture was done and bloody fluid obtained which contained 42.5 mg. of protein and 53 mg. of sugar per hundred cubic centimeters. Organisms were not seen in or cultured from the spinal fluid.

The patient was hospitalized and given alcohol rubs and ice packs. She was also given 2 Gm. of sulfadiazine and 0.5 Gm. every four hours intramuscularly, and subcutaneous administration of fluids was started. Her temperature fell to 101.6 F., and on the night of admission she had an especially severe spastic convulsion which was controlled with paraldehyde. Suction was repeatedly applied to the mouth and nose and her temperature again rose to 106 F. The child died on July 3, sixteen hours after admission. A clinical differential diagnosis of pyogenic meningitis, tuberculous meningitis or space-consuming cerebral lesion was made.

Necropsy.—An autopsy was performed on the day of death. The body was that of a well developed, well nourished white girl appearing about the stated age of 17 months. There were two small decubitus ulcers on the right buttock. There was a large thymus in the anterior mediastinal region. The remainder of the gross and the miscroscopic examination of the thoracic and abdominal organs revealed no particular abnormality.

The brain weighed 900 Gm. The convolutions were noticeably swollen. Just anterior to the optic chiasma, in the midline, a small (0.5 by 1 cm.) thin-walled sac, apparently bulging with fluid, could be observed. This was punctured and found to be the floor of the third ventricle, which was greatly dilated at this point. Approximately 100 cc. of clear cerebrospinal fluid was released through this opening. When the brain was raised from the skull, 8 to 10 cc. of necrotic deep red brain tissue resembling fine wet sawdust was left in the cerebellar fossa. The same material was noted to run about 3.5 cm. on the medial portions of both cerebellar hemispheres, extending up from the cerebellar surface as much as 1 cm. and involving the fourth ventricle, the meninges and the anterior and posterior surfaces of the pons and medulla (fig. 1). The two lateral ventricles were found to be uniformly and moderately enlarged, with atrophy of the cortex. A small soft, dark red mass was noted in the roof of the fourth ventricle just at the posterior medullary velum, which was occluding the lumen.

Microscopic Anatomy.—Study of the posterior and anterior horns of the right lateral ventricle, choroid plexus from a lateral ventricle and left motor cortex revealed no abnormality. An external granular layer of the cerebellum was not observed. A section through the pons and aqueduct of Sylvius revealed no tumor, but there was moderate dilatation of the aqueduct, with a few scattered tumor cells in the space between the cerebellum and a posterior corpus quadrigeminum. The inferior surface of the pons at this level showed a small piece of tumor in the midline. The bulk of this tumor was composed of closely packed round or pear-shaped cells with scanty, slightly acidophilic cytoplasm and large round or oval basophilic nuclei with fine chromatin. The cells were arranged in areas in pseudorosettes around a fibrillar material or around capillaries. There were, however, areas in which the cells were more sparsely placed. Here the cytoplasm was of a fine acidophilic fibrillar nature and extended out in one or two arms. There were areas of a network of this fine acidophilic fibrillar material with very few nuclei, especially noted around capillaries. In one area there was a strand composed of many cells with round nuclei and scanty cytoplasm; a network of the fine acidophilic fibrillar material bordered on both sides of the strand. At the edges of these bands, particularly at small capillaries, were a few hairlike spindle cells with more deeply acidophilic cytoplasm, with an elongated process directed toward the surface and with a flat oval more deeply basophilic or even a thin triangular-shaped nucleus.

Fig. 1.—Cerebellum with attached medulla and pons, showing the medulloblastoma extending out on both sides of the medulla and to the inferior surface of the pons.

A section from the cerebellum and fourth ventricle in the region of the posterior medullary velum contained numerous elongated, oval or bizarre-shaped adenomatous structures, some of which were visible to the naked eye. Some of these were lined with cells with scanty cytoplasm and mostly with round nuclei with fine chromatin; the cells were arranged in a single or stratified layer. The margins of such cells as these could not be definitely determined in hematoxylin and eosin or Wilder's silver preparations because of the scantiness of the cytoplasm and proximity of cells. Other adenomatous structures were lined by cells of a columnar or cuboid nature with round or oval nuclei situated in that portion of the cell away

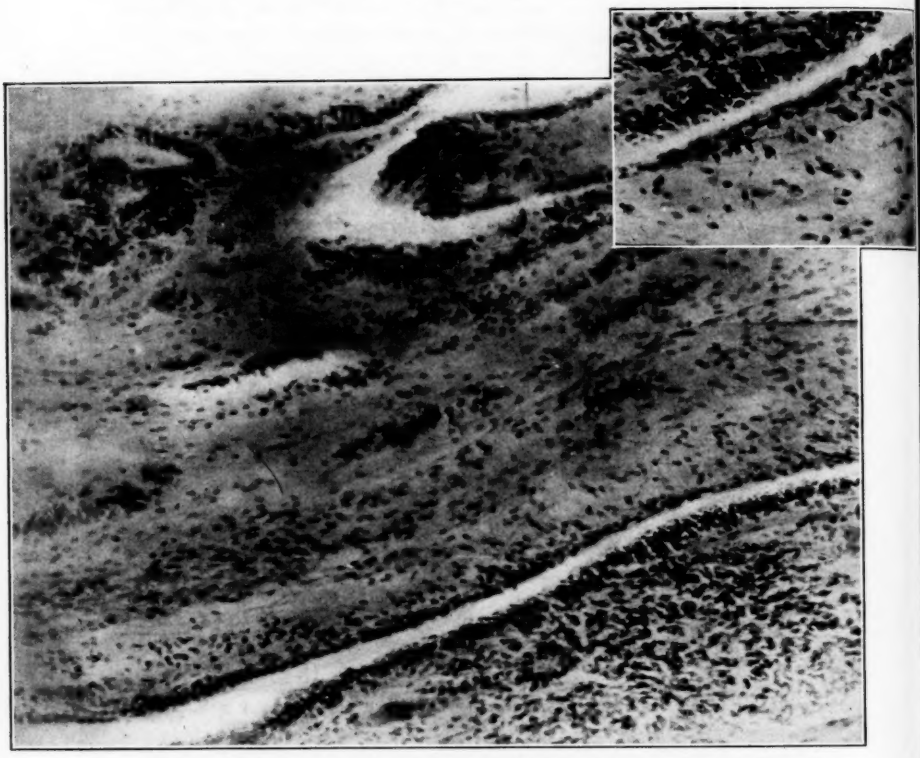

Fig. 2.—Cerebellum adjacent to the posterior medullary velum, showing the anomalous adenomatous structures. In the lower portion of the figure, a particularly long adenomatous structure is shown, one wall of which forms the outer limit of cerebellar substance. The other wall is part of the tumor, which occupies the lower right portion (× 66). The inset shows a higher power view (× 165) of the long structure, demonstrating the extension of tumor cells out from the wall.

from the lumen. The cytoplasm of these cells appeared to form a syncytium in some regions. Solid clumps of cells similar to those lining the glandlike anomalous structures were noted adjacent to the latter, and streams of similar cells were found sparsely scattered through the cerebellar substance of the section. These structures might extend up to the outer surface of the cerebellar substance, where the cellular

lining of several became continuous with tumor (fig. 2). Close to the cerebellum (fig. 2), the substance was similar to a medulloblastoma, whereas an abundance of acidophilic material was farther from the cerebellum (fig. 4, lower section). Another section of cerebellar tissue bordering on the posterior medullary velum also contained many adenomatous structures of a similar nature but smaller. Tumor growing from this section in one area was composed of the closely packed cells with round nuclei and scanty cytoplasm, forming pseudorosettes in areas. A segment of tela choroidea was infiltrated with tumor cells. Strands of tumor folded back on themselves in a U-shaped fashion, with round nuclei toward the periphery and cells with processes extending toward the central lumen, were seen (fig. 4, upper

Fig. 3.—A high power (× 300) view of an excellent pseudorosette and other formations found in this tumor.

section). A section taken from the cerebellum at the left tonsil just lateral to the vermis showed a tumor growing from the medial edge of the section which was composed entirely of the closely grouped cells with scanty cytoplasm and contained many pseudorosettes (fig. 3). At the point of origin of the tumor from the cerebellum were a few small adenomatous structures with their outer walls giving way to tumor as previously described (fig. 4, middle section). The cells of this rest wall were virtually identical with tumor cells at this point. A few mitotic figures were observed. A remarkable area of this section showed a schism into the tumor, lined with ependymal cells with cilia; another showed marked infiltration of the folium external to the internal granular layer.

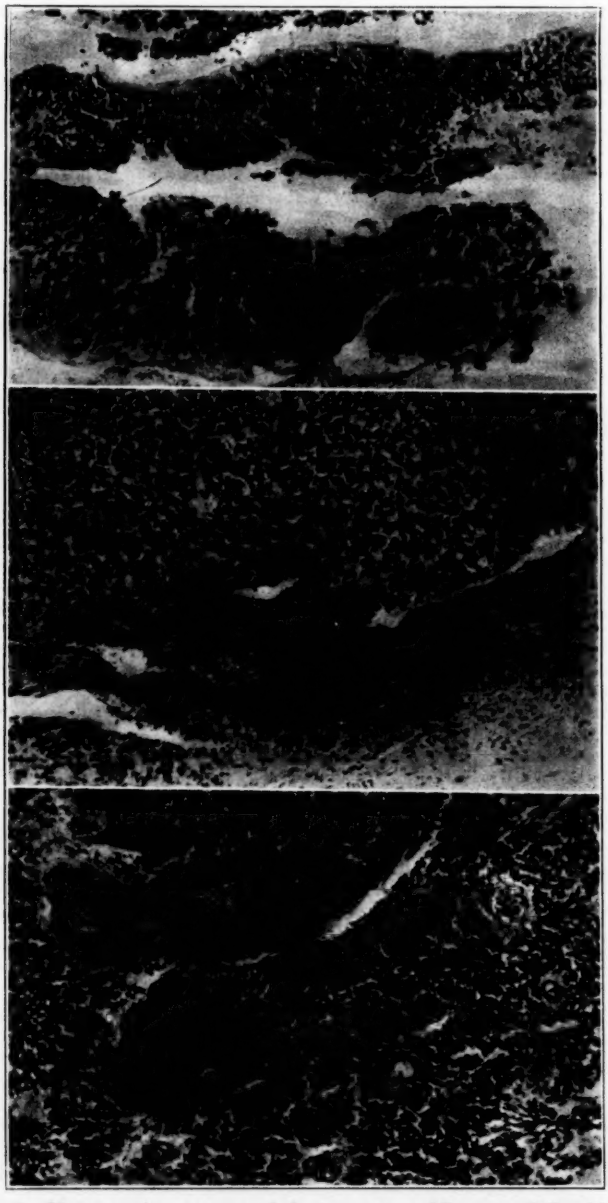

Fig. 4.—Upper section, an area of the tumor resembling a medulloepithelioma. Middle section, an area of the tumor showing some of the adenomatous structures that lined the cerebellum adjacent to the tumor. The majority of the tumor appeared as in this section. Note the pseudorosettes. Lower section, an area of the tumor resembling an ependymoblastoma. (× 60).

Progressive sections of the medial portions of the cerebellar hemispheres, vermis and medulla oblongata revealed the tumor to extend caudad from this last-described section and to take origin from the medial part of the left cerebellar hemisphere. It extended down to an area approximately lateral to the inferior vermis.

Those areas forming pseudorosettes, which were predominant, were thought to be typical medulloblastoma with perhaps a more primitive appearance of the component cells than usual; those forming the acidophilic fibrillar network were thought to resemble an ependymoblastoma, and those with strands of nuclei with processes toward the exterior, a medulloepithelioma. The adenomatous structures appeared to be rests composed of primitive cells, which were intimately associated with and adjacent to the tumor, with points where the tumor seemed to arise at a focus along the wall of the adenomatous rests.

The greatly variegated nature of this tumor, the unusual glandlike areas, the multiplicity of pseudorosettes, the areas simulating medulloepithelioma and ependymoblastoma indicate the multipotential structural factors involved. That this child was extremely young is undoubtedly a significant factor in the case. The examination of cells alone is not greatly impressive, and one wonders what primeval disorientation of organizers allows for the projections of such activity, ordinarily witnessed only in embryonal life, into the seventeenth postnatal month and from whence among the structures represented on the sections such chemical agents or causal factors of other nature emanated.

This case was interpreted as an instance of medulloblastoma, with elements simulating an ependymoblastoma and medulloepithelioma, which arose from primitive cells (medulloblasts) forming adenomatous structures or rests in an area of midline cerebellum adjacent to the posterior medullary velum.

COMMENT

Collections of abnormal cells in the cerebellum have been repeatedly encountered and reported, although it has not come to our attention that intimate and adjacent malignant degeneration has been noted. Raaf and Kernohan [3] noted abnormal collections of cells in the area of the posterior medullary velum in 23 of 104 embryos, fetuses or infants in which that region was studied. To support the derivation of medulloblastoma from such a site, they studied 25 cases in which the patient died of medulloblastoma. In all 25 cases the tumor was situated in the fourth ventricle. They stated the belief that in 16 it could be demonstrated that the tumor actually arose there, and in 8 of these microscopic study suggested that the tumor had its origin in the posterior medullary velum. These authors further remarked that Meschede encountered 3 examples of collections of abnormal cells in the cerebellum, that Wohlwill noted that a favorite site of rests was the roof

3. Raaf, J., and Kernohan, J.: Relation of Abnormal Collections of Cells in the Posterior Medullary Velum of Cerebellum to Origin of Medulloblastoma, Arch. Neurol. & Psychiat. **52**:163 (Sept.) 1944.

of the fourth ventricle and that Ostertag had commented on abnormalities in the cerebellum and the possibility that tumors might develop from them.

The occurrence of nervous diseases of the same type in identical twins has been cited as support of the idea of congenital origin of such diseases.[4] Such an occurrence of medulloblastoma in identical twins has been reported and cited as "evidence supporting the constitutional factor in and especially the 'fetal rest' theory of the development of neoplastic tissue." [5]

Brody and German,[6] in reporting their cases of medulloblastoma, subscribed to this idea of embryonal origin. They reported finding in 1 case of this tumor small cystic areas in the tumor containing mucilaginous material but no definite stroma.

Certainly the fact that this tumor most frequently arises in the midline of the cerebellum just over the fourth ventricle,[7] the point where the embryonal rests are most often observed, is strongly in favor of the origin of the tumor from such cellular groups. However, there are a few cases reported in which the material would demonstrate origin from the folia of the cerebellar hemispheres. Two cases especially (in patients aged 29 and 16 years) have been described [8] in which a tumor similar or identical to medulloblastoma arose, not from the roof of the fourth ventricle or vermis, but from the folia of the hemispheres, where the authors demonstrated it was growing from the outer surface of the leaflets and separating them. In some parts of one of the tumors, adjacent to the neoplasm, there was what appeared to be remnants of an external granular layer. Stevenson and Echlin presented 4 other cases in which the tumor cells were said to resemble those of the external granular layer.

Scheinker [9] reported an interesting case of tumor in a 49 year old man; histologically it was a medulloblastoma, arising with persistence of the Obersteiner layer. The tumor was primarily in the vermis. Scheinker expressed the opinion that the tumor probably arose from cells of the Obersteiner layer. This case and the first 2 cases described

4. Wilson, S. A. K., and Wolfsohn, J. M.: Organic Nervous Disease in Identical Twins, Arch. Neurol. & Psychiat. **21**:477 (March) 1929.

5. Leavitt, F. H.: Brain Tumors in Childhood: A Clinicopathologic Study, Am. J. M. Sc. **178**:229 (Aug.) 1929.

6. Brody, B. S., and German, W. J.: Medulloblastoma: Fifteen Cases, Yale J. Biol. & Med. **6**:19 (Oct.) 1933.

7. Bailey, P.: Intracranial Tumors, Springfield, Ill., Charles C Thomas, Publisher, 1933, p. 227.

8. Stevenson, L., and Echlin, F.: Nature and Origin of Some Tumors of the Cerebellum: Medulloblastoma, Arch. Neurol. & Psychiat. **31**:93 (Jan.) 1934.

9. Scheinker, I.: On the Question of the Pathogenesis and Pathology of the Medulloblastoma, Monatsschr. f. Psychiat. u. Neurol. **101**:103 (May) 1939.

by Stevenson and Echlin as occurring in the cerebellar leaflets and associated with apparent remnants of the external granular layer are probably sufficient evidence that the medulloblastoma in some instances is derived from the cells of the Obersteiner layer. It is interesting to note that 2 of these cases are examples of medulloblastoma in an adult and 1 of its occurrence in a 16 year old adolescent.

Most of the criticism of the origin of the medulloblastoma from heterotopic cellular rests composed of medulloblasts lies in the beliefs of the nature of the cell composing the tumor. It will be recalled that Bailey and Cushing [1] described this cell as undifferentiated and similar in nature to the *indifferenten Zellen* of Schaper, an apolar cell capable of differentiation into neuroblasts or spongioblasts, which they named the "medulloblast." These authors described, in addition to the medulloblasts, a few neuroblasts and many more spongioblasts in their tumors. However, Bailey [10] later expressed the thought that "especially hypothetic are the medulloblasts." Others (Roussy, and Roussy and Oberling [11]) concluded that neuroblasts and not the indifferent cell of Schaper are the preponderating cell elements of the tumor, although they also found occasional spongioblasts (Roussy, Oberling and Raileanu [12]). Marburg, according to Winkelman,[11] believed that the medulloblastoma could be eliminated from the glial group because of the presence of connective tissue within the lesions. While Stevenson and Echlin [8] have expressed the belief the medulloblastoma is derived from the external granular layer, they have stated the "external granules are neuroblasts," not medulloblasts, and proposed to name the tumor neuroblastoma or granuloblastoma.

The Obersteiner, or external granular, layer is derived from proliferating cells extending out from the rhombic lip over the surface of the cerebellum after the masses of the cerebellar hemispheres have formed from the cerebellar alae lying in the anterior walls of the fourth ventricle.[13] This occurs during the third embryonal month, and the actual extension can be demonstrated to proceed from a dense cellular rest at the posterior tip of the roof of the fourth ventricle.[14] The external

10. Bailey, P.: Histologic Atlas of Gliomas, Arch. Path. **4**:871 (Dec.) 1927.

11. Winkelman, N. W., and Eckel, J. L.: Midline Cerebellar Tumors ("Medulloblastoma"): A Clinicopathological Report of Cases Showing Diffuse Dissemination Throughout the Central Nervous System, Surg., Gynec. & Obst. **63**:372 (Sept.) 1936.

12. Swan, C.: A Clinico-Pathologic Study of Eight Cases of Medulloblastoma and of One of Spongioblastoma Ependymale Simulating Medulloblastoma, M. J. Australia **2**:153 (Aug. 12) 1944.

13. Arey, L. B.: Developmental Anatomy, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 437-439.

14. Kershman, J.: The Medulloblast and the Medulloblastoma: A Study of Human Embryos, Arch. Neurol. & Psychiat. **40**:937 (Nov.) 1938.

granular zone may persist almost to the end of the first year of postnatal life. To clarify the existence and nature of the medulloblast and the identification of the cells of this external granular layer, Kershman undertook an extensive study of human embryos.[14] He noted a constant flow of cells from the external granular zone from the time of its earliest formation. Until the time of birth, the migrating cells consisted almost exclusively of round or oval elements, which culminated in the formation of mature internal granule cells. From birth he found that two distinct cell types emanated from the external granular layer, one of which developed into basket cells and the other into Golgi-Bergmann and Fannanás astrocytes. The Obersteiner layer thus gave rise to neurocytes and glial cells, and Kershman concluded that they were undifferentiated, bipotential elements, thus satisfying the criteria of Schaper's indifferent cell, which may then be called a medulloblast. He found no evidence of medulloblasts in any part of the brain or spinal cord except the cerebellum, thus indicating why the tumor is confined to the cerebellum.

From this work, it would appear that those tumors derived from Obersteiner's layer, in which the cells resemble the external granular layer, are composed in part of medulloblasts. The cells of the tumor we described correspond to primitive cells or to the medulloblasts as originally described by Bailey and Cushing.[1] The multipotentiality of the cells is indicated by the character of the tumor. In the face of these facts and the conclusions derived from the work of Kershman, it would perhaps not be incompatible to feel that those tumors derived from heterotopic rests are likewise composed of medulloblasts and that the cells of the heterotopic rests are medulloblasts or other similar primitive cells.

SUMMARY AND CONCLUSIONS

A case is reported in which adenomatous rests in the cerebellum at the roof of the fourth ventricle apparently gave rise to medulloblastoma.

From the literature there is ample evidence of the existence of cellular rests in the cerebellum, but we have noted no previous case demonstrating neoplastic change into medulloblastoma.

It appears from an evaluation of the literature that medulloblastoma may arise from a persistent external granular layer—these granule cells are probably medulloblasts—and that it may arise from any point where there is such a layer, not necessarily at the vermis.

It may be concluded from this case and earlier reports in the literature that both the external granular layer and embryonal rests of the cerebellum may give rise to medulloblastoma.

University Hospital.

Correspondence

"CLINICAL EXAMINATION OF THE NERVOUS SYSTEM"

The accompanying correspondence concerned with Dr. Wartenberg's review of "The Clinical Examination of the Nervous System," by G. H. Monrad-Krohn, published in the April 1949 issue of the ARCHIVES, *is self explanatory.*

Dear Professor Wartenberg:

The same mail which brought me the April issue of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY also brought me your letter in which you invite me privately and/or publicly to tell you whether I feel that you have wronged me in your review of my "Clinical Examination of the Nervous System."

At your invitation, therefore, I shall venture a few remarks. Your most serious accusation against me is that I have indulged too much in local Norwegian patriotism in my quotations and references. I feel exceedingly sorry to learn that my book may create such an impression and am therefore eager to explain the genesis of this apparent overpatriotism:

I have myself always liked a personal book, in which the author, at least to a certain extent, documents what he himself can vouch for. Now this book of mine is not a mere compilation of tests, but a book based on the experience gained in my own clinic, where many methods have been put to the test by myself and my assistants. This is the reason that so many references to this work of my own clinic are given—without any intention of claiming any undue priority or any undue merit. A complete bibliography is, of course, not intended.

When you reproach me that on page 151 I still use the term "tendon and periosteal reflexes," I think it is fair to mention the *whole* head line on page 151 of my book, viz., "Tendon and Periosteal Reflexes (Deep Reflexes, Phasic Myotatic Reflexes)," with the following footnote, "Gowers already in 1881 proposed the name 'myotatic contractions' for these reflexes. In his textbook of 1886 he writes: 'A tap on the tendon itself only excites the contraction when it increases the tension of the tendon—i. e., when it acts upon the muscle also.' "

On the following pages I explain the physiologic mechanism, emphasizing that the responding muscles represent both the receptor and the effector organ. Here, also, I explain that some of these myotatic reflexes are labeled after the tendon or periosteal region where the eliciting tap is applied. This is still done in most of the clinics I know. The names used by me are so firmly established in the neurologic terminology that they will not easily be dislodged, nor do they signify any ignorance of the physiologic mechanism on the part of the neurologists who still use them. No student will have any excuse for such ignorance after having read pages 151-154 of the eighth edition of my book (pages 181-183 of the ninth edition, just out). I think you will agree if you read those few pages once more. I am fully aware of your attempt to introduce new names for the deep reflexes and fully appreciate your reasons for this. When I have not followed you in this, it is partly because I think that the names employed by me and by many others cause no confusion and chiefly because *many of these myotatic reflexes have a pluri-muscular response.* To name them after one muscle may therefore also be misleading to some extent. For example, in the radialis periosteal reflex there is a response not only of the brachioradialis, but often also of the biceps—and even of the finger flexors. In eliciting the patellar reflex, one often notices the adductors contract as well, etc., etc. It is therefore of importance that the examiner note how far—to how many different muscles—the contraction spreads. If these reflexes had been strictly unimuscular reflexes, I think it would be an advantage to adapt your new names and speak of the brachioradial reflex instead of the radialis peri-

osteal reflex. But as they are not, I have hitherto not found it of any practical advantage to adopt the Wartenberg terminology, although I am fully aware of your physiologic reasoning.

To state, as you do, that "there is no such thing as the periosteal reflex of the costal margin" is equal to saying that "there is no such thing as a patellar reflex" or "there is no knee jerk" or "there is no ankle jerk." One cannot deny the existence of a phenomenon because one does not like the name given to it. The periosteal reflex of the costal margin, as described in my textbook, does exist; and it is listed, as it ought to be, under the heading "Tendon and Periosteal Reflexes (Deep Reflexes, Phasic Myotatic Reflexes)" with the full physiologic orientation, previously alluded to.

To infer that the reflex formulas on page 198 should mislead the student "to make a differential diagnosis between hysteria and organic lesion on the behavior of the reflexes!" is to my mind not quite fair. If you have read the preface, as no doubt you have, you will find it emphasized that it is "the systematic evaluaton of the constellation of pathological findings" that forms the basis for diagnosis. If a student be misled by the "reflex formulae" on page 198 to such a diagnostic attempt as you suggest, his I. Q. must be so low that he will never be fit to become a physician. I agree, however, that "hysterical lesion" had better be altered to "hysterical disturbance," but the tabulated "reflex formulae" indicate only that such reflex findings *may* be present with the different typical lesions. They must be understood *cum grano salis.* Thus no student, I hope, would be led to expect an extensor plantar response in a case of isolated pyramidal paralysis of the upper limb.

I have indulged in certain digressions in order to enliven and illustrate the dull description of examination technic a little. This I think justifiable, even if our tastes differ in this respect. Thus, the two short footnotes on pages 32 and 74 which you mention are to my mind hardly out of place. Such modest references may have their value and are found in most textbooks.

The illustrations, practically all from my own clinic, have been chosen with the double aim of illustrating (1) things that are important and (2) things that the beginner is apt to overlook.

Any lack of balance in the choice of these as in the subject matter—in keeping with the author's correspondingly more or less balanced mind with interest focused on pet subjects—is not for me to discuss. (May I in attenuation mention that I have seldom read a book worth reading without discovering the author's pet interests, even when possibly better concealed than my own. Also, the relative stress paid to different points varies considerably from clinic to clinic.)

Finally, I must own that the blame for any linguistic *gaucherie* that you think you have discovered cannot be put down to a nonexisting translator, as I wrote the book myself in English.

For some of your criticism, e. g., that regarding the Strümpell phenomenon, where you are quite right, I am truly grateful. I shall bear it in mind if and when the tenth edition is needed. Unfortunately, the ninth English edition is already out, so I am debarred from benefiting by it for this edition. It is the eighth edition you have reviewed. This has already been reviewed in the ARCHIVES. I wonder why a second review of the same edition was needed.

I note with profound gratitude that, in spite of all, you still find that my "Clinical Examination of the Nervous System" is "indeed a good book." I shall endeavor to make it still better if future editions are needed, and shall then take the constructive part of your review into consideration.

Reciprocating your friendly greetings, I am

Yours sincerely,

G. H. MONRAD-KROHN, M.D., F.R.C.P., Oslo, Norway.

News and Comment

COURSE IN CHILD PSYCHIATRY, CENTER FOR CONTINUATION STUDY

A course in child psychiatry will be presented at the Center for Continuation Study, Chicago, on Nov. 28 through Dec. 3, 1948. This continuation course, which is intended for pediatricians and general physicians, will emphasize normal, emotional, intellectual and social development of infants and children and the emotional and behavior problems seen in infancy, childhood and adolescence. Dr. Adrian Vander Veer, of the department of psychiatry of the University of Chicago, will participate as a visiting faculty member.

THIRD ANNUAL CLINICAL SESSION OF THE AMERICAN MEDICAL ASSOCIATION

The Third Annual Clinical Session of the American Medical Association will be held in Washington, D. C., December 6 to 9.

The Clinical Session will provide a full scale scientific program specifically designed for the general practitioner. Outstanding physicians will discuss such subjects as diabetes, pediatrics, laboratory diagnosis, physical medicine and rehabilitation, arthritis, dermatology, roentgen ray diagnosis, cancer and poliomyelitis. Coordinated with this notable scientific program will be approximately one hundred scientific exhibits which will present original work on the subjects discussed.

The newest offerings of one hundred and twenty-five manufacturing firms will comprise the Technical Exhibition. Here will be found the latest developments in scientific medical research, drugs and equipment.

Televised surgical and clinical procedures, similar to those shown in color at the Annual Session of the American Medical Association in Atlantic City last June, will be presented at the Washington meeting. The demonstrations will originate in the Johns Hopkins Hospital and will be shown on screens in the Armory. The television schedule will be spread over four days.

The House of Delegates will meet at the Hotel Statler during this session. One of the first orders of business will be the annual selection of the general practitioner who has made an exceptional contribution of service to his community.

An entertainment program for attending physicians and their wives is being planned. The highlight of this program will be on Wednesday evening, December 7, when Philip Morris' "This Is Your Life" will be broadcast from the Hotel Statler. The radio program will be followed by a stage show, in which outstanding stars will participate.

Blanks for hotel reservations and advance registrations may be found in *The Journal of the American Medical Association.*

CORRECTIONS

In the article by Drs. Robert Hodes, M. G. Larrabee and W. German entitled "The Human Electromyogram in Response to Nerve Stimulation and the Conduction Velocity of Motor Axons: Studies on Normal and on Injured Peripheral Nerves," published in the October 1948 issue of the ARCHIVES, an error appears on page 348, beginning in the sixth line. The sentence "The change in latency when divided by the distance between the two points of stimulation yielded an accurate measure of the conduction velocity of the most rapidly conducting fibers" should read: "The distance between the two points of stimulation when divided by the change in latency yielded an accurate measure of the conduction velocity of the most rapidly conducting nerve fibers."

In the article entitled "Relation of Changes in Carbohydrate Metabolism to Psychotic States" by Harry Freeman, M.D., and Ralph N. Zaborenko, M.D., published in the May issue of the ARCHIVES, page 569, the second author's name should read Ralph N. Zabarenko.

Abstracts from Current Literature

Physiology and Biochemistry

EXCHANGES OF SODIUM AND POTASSIUM IN FAMILIAL PERIODIC PARALYSIS. T. S. DANOWSKI, J. R. ELKINTON, B. A. BURROWS and A. W. WINKLER, J. Clin. Investigation **27**:65, 1948.

The authors studied 2 cases of familial periodic paralysis. Quantitative data on 1 case was obtained during recovery from a spontaneous attack of generalized paralysis. In the first period, of three hours, potassium chloride was given by mouth; in the succeeding period, of sixteen hours, the patient took food and water. The study in the other case extended over a period of four days, during which an attack of paralysis was induced by withdrawal of the maintenance dose of potassium chloride and administration of large doses of carbohydrate. The patient received no other food during the entire study. Recovery was effected by giving potassium chloride intravenously and orally. The potassium, sodium and water exchanges, as well as electrocardiographic alterations, were studied.

The results indicated that the movement of potassium associated with the onset of muscular paralysis consisted in a transfer of extracellular potassium into the intracellular phase, with a striking depression of extracellular concentration resulting. Calculated balances were for the over-all phases and did not differentiate the distribution in the various tissues. The authors ascribed the transfer of potassium to the cycle of carbohydrate combustion in skeletal muscle. The primary cause of the paralysis was thought to be the loss of potassium from the extracellular fluid, the resulting low concentration producing an effect on the neuromuscular mechanism. The concurrence of hypopotassemia and muscular weakness in other clinical and experimental conditions was pointed out. During recovery large amounts of administered potassium were taken up by the intracellular phase before the extracellular phase was replenished.

In the one patient during recovery some sodium shifted from the extracellular to the intracellular phase at the same time that the potassium was being taken up into both phases. In the other patient a reciprocal relation between sodium and potassium appeared, with the amount of cellular sodium increasing slightly during the initial diminution of cellular potassium, and a reverse relation was noted during the recovery period, when potassium entered cells.

No significant changes occurred in the volumes of total body water and extracellular fluid.

Electrocardiographic alterations were consistent with the known effect of low concentrations of serum potassium, with absence or inversion of T waves in lead 2 and minor changes in S-T segments during paralysis. Normal records were obtained during recovery.

DONALD, Philadelphia.

THORACIC, LUMBAR, AND SACRAL SPINAL CORDECTOMY. COLLIN S. MACCARTY and EDWARD J. KIEFER, Proc. Staff Meet., Mayo Clin. **24**:108 (Feb. 16) 1949.

MacCarty and Kiefer were encouraged to perform chordectomy in a case of malignant tumor of the spinal cord by the recognition through previous work of Shelden and Bors that bladder and bowel functions can be reestablished after

destructive procedures involving the cauda equina. The spinal cord was transected first in the thoracic region and, at the same operation, at the seventh cervical segment. At a subsequent operation the cauda equina was sectioned and the conus medullaris removed. Another operation was performed for further removal, so that by the time of completion of this procedure the entire spinal cord had been removed from the seventh cervical segment through the cauda equina. At the first segmental resection 11 cm. was removed; at the second, 1 cm. plus 11 cm. of cauda equina; and at the third, 24 cm. of spinal cord.

ALPERS, Philadelphia.

TROPHOKINETIC ROLE OF THE ANTERIOR PORTION OF THE DIENCEPHALON: PRELIMINARY NOTE. A. MANCEAU, A. M. LARMANDE and M. JORDA, Encéphale **37**:308, 1948.

Roussy and Mosinger, in their treatise on neuroendocrinology, sustained the view that "the hypothalamus represents the reflex center by means of which the external world, the psychic life of the individual and the viscerosensory influx make their influence felt on the morphologic constitution of the organism." This regulating apparatus controls what these authors called the "trophokinetics" of the organs and tissues. The authors of the present paper believe that they can bring proof of the trophic and dynamic action of the diencephalon on nerve elements themselves—to wit, on the anterior optic pathways. Their studies were made in the course of experimental work on the various functions of the diencephalon, in which they used guinea pigs with lesions localized in the subthalamic region. The histologic material of the chiasm was stained according to the technic of Romanes (1946).

The authors state that their first series of studies indicates that a lesion of the anterior portion of the diencephalon, provided it is bilateral, is quite capable of causing atrophy of the optic fibers and proliferation of the glial elements after three weeks. This fact, they feel, proves the trophic effect of the diencephalon on the sensory elements of the optic pathways, which were not at all involved in the lesion created experimentally. It is the tangention retinal pathway postulated by Roussy and Mosinger which controls the trophic action on the peripheral nerve elements.

ZINKIN, Fort Worth, Texas.

MECHANISM OF ORIGIN OF LASÈGUE'S SIGN. OLOF SJÖQVIST, Acta psychiat. et neurol. (supp.) **46**:290, 1947.

Sjöqvist studied 5 cases of herniation of the intervertebral disk. In all cases there was a positive Lasègue sign on at least one side, with a crossed Lasègue sign in 3 cases. Myelographic studies in all cases showed a defect in the dural sac. Operations were performed under local anesthesia with the patient in the lateral position. On exposure of the field after laminectomy the Lasègue test was performed, with positive results obtained in all cases. Thereupon injection of procain was made into the root or roots which were compressed by the herniated disk. Repetition of the test for Lasègue's sign then gave negative results. Stretching of the nerve root in a caudal direction was noted on performance of the test, and pressure exerted by the protruding disk was increased with tension. The author concluded that the sign of Lasègue is neural in origin and is produced by purely mechanical factors.

DONALD, Philadelphia.

BLOOD-BRAIN BARRIER IN CONCUSSION. D. ENGEL, Acta psychiat. et neurol. **23**:231, 1948.

In 10 cases of acute cerebral concussion Engel found increased permeability of the blood-brain barrier. Dye appeared about two hours after intake, by both the fuchsin and the fluorescein method. No excretion of dye was found in 8 cases of chronic cerebral trauma. Engel concludes that only in cases of acute concussion is the permeability of the blood-brain barrier increased.

ALPERS, Philadelphia.

Neuropathology

TUMORS OF PERIPHERAL NERVES, WITH SPECIAL REFERENCE TO NEUROGENOUS SARCOMAS. E. BUSCH and ERNA CHRISTENSEN, Acta psychiat. et neurol. 1947, supp. 46, p. 72.

Busch and Christensen review the classifications of tumors of peripheral nerves and discuss 6 patients with such tumors. No clinical difference was found in the benign predominantly ectodermal tumor (neurinoma), the benign mesodermal neurofibroma and the malignant mesodermal sarcoma. The duration of illness varied from three months to six years. The symptoms consisted of paresthesias, and sometimes of central disturbances, paralysis in cases in which a motor nerve was affected. Four tumors were located in the lower extremities and 2 in the upper. The youngest patient was 27 years old and the oldest 72, with a ratio of women to men of 2:4. Operation, with removal of the tumor, was performed in all cases, with recurrence of the tumor in 2 cases. A second operation was performed in the latter with bloc extirpation of normal tissue and the affected part of the nerve. Postoperative roentgen treatment was then given. Comparison of the sections from the tumors which required repeated operation showed an unquestionable change toward malignancy in the histologic features. Study of the specimens revealed 2 neurinomas and 2 neurosarcomas (spindle cell type). In the 2 cases with recurrences, the first tumor removed was a neurofibroma, whereas sections from the tumor removed at the second operation were typical of spindle cell sarcoma. One tumor underwent further malignant change with recurrence, and sections from the specimen obtained in the third operative procedure were classed as polymorphocellular sarcoma. Busch and Christensen state the belief that tumors of the peripheral nerves which prove to be neurofibromas must be considered as malignant, even though no definite signs of malignancy can be demonstrated histologically. They recommend postoperative roentgen treatment, in addition to a careful en bloc excision of the tumor.

DONALD, Philadelphia.

HISTOPATHOLOGIC REACTION OF THE AREA POSTREMA. JAN CAMMERMYER and RAYMOND D. ADAMS, Acta psychiat. et neurol. **23**:205, 1948.

In a study of the area postrema in 130 cases of pathologic conditions, it was found that a variety of changes occur from birth to old age. Nerve cells originally located at the ventrolateral base are later displaced toward the ependymal surface, and their arrangement, at first suggestive of glandular structure, is less apparent later. At about 15 years of age an intracellular granulation of lipid nature begins to appear in the nerve cells. At 25 years of age melanin appears. Both these substances increase with age. Microglia cells and immature forms of neuroglia cells which appear beneath the ependyma in early life tend to disappear after a few months and do not reappear in significant number except in disease.

Ventricular and subarachnoid hemorrhages result within six days in deposit of hemosiderin in the leptomeninges, the choroid plexus and the area postrema.

Trauma of the brain may cause petechial hemorrhage in the area postrema. Infectious diseases frequently cause an inflammatory process in this area, as well as in the subarachnoid space.

ALPERS, Philadelphia.

Psychiatry and Psychopathology

SOME OBSERVATIONS ON THE ANALYTICAL GROUP TREATMENT OF A PHOBIC PATIENT. F. KRÄUPL, J. Ment. Sc. **94**:77 (Jan.) 1948.

Kräupl examines in some detail the response of a man aged 38 to analytically oriented group psychotherapy to gain evidence concerning treatment group dynamics. The group consisted of seven to nine men and gathered once a week. Each patient had had personal attention prior to joining the group, but no individual sessions were given during the course of collective meetings.

The patient had been raised in a puritanical household and had always avoided women. Holidays were spent with male friends, and after his last trip as a bachelor he experienced a travel phobia, which later spread and greatly restricted his living. He married at 26 and had two children. For years he had been tormented by daydreams of perverse sexual practices, largely sadistic in tone. Anal-erotic tendencies were traced back to childhood enjoyment in the insertion of soap suppositories. The psychosexual constitution showed repressed passive homoerotic impulses. In his individual treatment hours the patient eagerly unburdened himself and confessed his guilt-charged fantasies. He derived some relief from a tolerant reception of his revelations, but his symptoms remained unaltered.

The patient attended the therapy group for fourteen months. It was many weeks before he took an active part. Gradually, through discussion of his masturbation fears, sexual fantasies, dread of his father, anal pleasures and passive sexual drives, he lost most of his irrational social phobias, evidently by reduction of guilt feelings and gradual acceptance of his passive feminine and masochistic leanings. The travel phobia did not respond so satisfactorily, and he continued to have sexual fantasies, mostly of a masochistic nature, but now without censuring himself. He discontinued group therapy on his own volition and several months later resumed individual therapy.

The author discusses the factors responsible for the partial success in this case. The group task of self revelation was a stimulus to his exhibitionism, and disclosures concerning his sexual life were corrective experiences with cathartic value. Sexual discussions in the completely male group seem to have been a substitutive gratification for his homoerotism. It is not believed that the group experiences are true transference phenomena, since emotions which emerge are always adequate to the actual environment. It is conceived that the group is a social reality which can relieve guilt feelings by the reassurance of acceptance and by diminution of the fear of being different and abnormal. This is particularly true of neuroses the symptoms of which appear in a social context. That group therapy in this sense is more realistic than individual therapy may partially explain the greater intensity of emotional response. In the case reported only partial insight was achieved, and insight is apparently not a necessary attribute of the group effect. The method has limitations, as here observed; and the therapeutic range differs from that of individual treatment and is determined by the group setting. Only such reactions as have an echo in the general collective atmosphere can be benefited, and unconscious levels are therefore accessible in limited degree only. Research with groups of varying compositions is suggested to evaluate the compass of the technic.

BEATON, Tucson, Ariz.

LUNG ABSCESS FOLLOWING ELECTRO-CONVULSIVE THERAPY. HUGH CONWAY and HUMPHRY OSMOND, J. Ment. Sc. **94**:653 (July) 1948.

Inhalation pulmonary abscess is one of the little emphasized dangers of electric shock treatment. The actual incidence is not known, but the condition is apparently rare, judging from the paucity of reports in the literature. It is generally agreed that preexisting pulmonary disease, especially tuberculosis, is a strong contraindication to the therapy. Of persons undergoing metrazol® convulsion, in whom there is an additional risk of embolic abscesses due to mobilization of thrombus at the site of injection, the complication is said to occur in 0.1 per cent.

The case reported is that of a Maltese aged 32 with a provisional diagnosis of catatonic schizophrenia. The roentgenogram of the chest was normal, but examination disclosed Vincent's infection of the mouth. This was cleared with potassium bichromate and hydrogen peroxide. Five shocks were given in seventeen days, and from the very beginning of treatment the patient showed a decided change for the better. On the twentieth day, however, cough, pain in the chest and purulent sputum developed, associated with fever and scattered rhonchi. Roentgenographic study revealed an abscess of the upper lobe of the left lung. Postural drainage and administration of penicillin resulted in improvement, although it was two months before all consolidation in the lung disappeared. During the period of convalescence from the pulmonary infection the patient relapsed into catatonia.

The authors believe that the abscess was inhalational and stress the potential hazards of inflammation of the mouth or dental disease and the need for thorough oral examination prior to electric shock therapy. The normal roentgenogram of the chest prior to treatment in this case served to rule out tuberculosis and so precluded what might have been a dangerous delay in the institution of proper management of the abscess. This complication affects the prognosis adversely because the convulsive therapy must be abandoned. A vicious circle is then established, since the reduced activity of catatonia militates against ultimate recovery from the infection. In dealing with persons who have undergone shock treatment, the physician must not ignore what appear to be minor complaints. A serious organic lesion may be present in an uncooperative or apathetic subject with few physical signs and little systemic involvement.

BEATON, Tucson, Ariz.

ANALYSIS OF POSTURAL BEHAVIOR. FELIX DEUTSCH, Psychoanalyt. Quart. **16**:195 (April) 1947.

Deutsch states that during psychoanalysis the motor behavior of patients can be observed to be motivated by underlying and coordinated psychologic processes. Postural attitudes reflect or substitute, precede or accompany the verbal expression of unconscious material. Each patient has a characteristic basic posture at rest, to which he returns whenever he has deviated from it. This characteristic posture appears immediately or soon after the analysis has begun. Posture changes whenever a shift in the analytic process takes place for which another postural expression is needed. These new postures are released through the emergence from repression of unconscious material. Postural reaction may express either anxiety or its repression. Movements seem to aim at the release of tension and are repeated until the tension is adequately discharged.

The author expresses the conviction that observation of postural patterns furnishes the analyst with additional clues to psychodynamics. The better acquainted he is with the basic postural pattern of a patient, the more readily apparent significant and indicative will deviations from this pattern become to him.

WERMUTH, Philadelphia.

PHALLIC WOMEN. SMILEY BLANTON, Psychoanalyt. Quart. **16**:214 (April) 1947.

Blanton points out that there is a fundamental antagonism between men and women. The unconscious fear of women in men is based on the early distortion of fact that to men women are castrated and that where the penis is in man is a place in woman where blood issues from time to time. Another reason for this fear is man's infantile dependence on his mother for care and love. Independence of his mother is comparatively simple for the boy as compared with the girl, for he has only to shift his love to another woman, whereas a girl has first to turn from the mother to the father. If a mother excessively dominates a daughter, the resolution of the Oedipus complex fails, with consequent infantile fixation on the mother rather than a healthy identification with her. Such dominating mothers often have the unconscious fantasy of having a penis; to a certain extent this fantasy in women is imposed by male phallic narcissism. The envy centering around the possession of a penis and the castration complex must come from overevaluation of masculinity or be imposed on women by compensatory masculine overevaluation of the penis.

The author describes a type of phallic woman quite feminine in appearance and attitude and eager to appear to respond in sexual relationships with men. Such patients usually react favorably to psychoanalysis if they are not so old as to become too deeply fixed in a rigid reaction of habit. They are often able to make an ideal psychosexual adaptation following the analysis of a castration anxiety in the setting of the infantile neurosis.

WERMUTH, Philadelphia.

SOME PSYCHOSOMATIC ASPECTS OF THE MANAGEMENT OF SURGICAL PATIENTS. MACK LIPKIN and EDWARD JOSEPH, Surgery **25**:268 (Feb.) 1949.

Lipkin and Joseph discuss the manner in which the surgeon and his associates can help to overcome the anxiety connected with any operation. During the preoperative interview, the patient's fear of death, disfigurement, disability and financial worries are met with reassurance and encouragement. The anesthetist may help to comfort the patient before operation. Anesthesia given while the patient is in bed will help to prevent anxiety. If spinal anesthesia is used, the patient's eyes should be covered and conversation guarded. The patient is benefited by the surgeon's visits, individualization of drugs and feedings and early ambulation after the operation. The surgeon can manage postoperative depressions by meeting them frankly and sympathetically; the psychiatrist need enter the picture only when the patient becomes frankly psychotic. During convalescence, the patient is best allowed maximum activity and as little dietary restriction as possible; vacations may not be of much value.

FRANKEL, Philadelphia.

SCHIZOPHRENIA AND RETINITIS PIGMENTOSA. A. STEINHARDT, Harefuah **33**:103 (Sept. 14) 1947.

Steinhardt reports the case of a woman aged 30 whose parents were related. Retinitis pigmentosa had been present since childhood and resulted in almost complete blindness. There were a history of retinitis pigmentosa in 2 siblings and a family history of mental disease and epilepsy. The schizophrenic syndrome, which began at the age of 20, was remitting, with catatonic features and a reactive depression. The patient was given a course of insulin therapy. The author gives no definite opinion as to the relation of the retinitis pigmentosa to the schizophrenia. He emphasizes the necessity of recording such cases because of the obscure nature of both diseases.

N. SAVITSKY, New York.

Meninges and Blood Vessels

DIFFUSE PRIMARY MENINGEAL SARCOMATOSIS. J. C. ORTIZ DE ZARATE and T. INSAUSTI, Rev. asoc. med. argent. **61**:795 (Nov. 15) 1947.

The authors report a case with onset of the illness forty days prior to the patient's admission. Weakness, vomiting and headaches occurred for about a week. The patient was then well for about eight days, when he began to vomit again, and during the next twenty-five days he complained of dizziness and headaches. He then had a seizure, followed by diminished vision on the right, bilateral diminution of hearing and double vision. The course was afebrile. During severe exacerbations of headache he could not speak. On admission, he showed meningeal signs, hyperalgesia of the skin, tenderness of the cervicothoracic region of the spine, a bilateral Babinski sign, deafness and bilateral choking of the disks with hemorrhages. Lumbar puncture revealed an initial pressure of 80 mm. of water; the fluid was clear, and there were 1.3 cells per cubic millimeter; the protein content was normal; no tubercle bacilli could be demonstrated, and the Huddleson reaction was negative. Iodoventriculograms showed small ventricles, probably due to edema of the brain. A subtemporal decompression done on the right side soon after the patient's admission revealed a subdural mass, in which biopsy revealed inflammatory tissue. The patient died twenty-one days after the operation. Autopsy showed masses in the left frontal and left parietal regions of the brain with an intracerebral hemorrhage in the central white matter of the right frontal region. The ventricles were small, and the meninges were thickened and gelatinous with scattered granulations. There were leptomeningeal hemorrhages in the right temporal and frontal regions and in the frontal pole. Histologic examination showed diffuse meningeal sarcomatosis with metastatic nodules in the brain. The authors reviewed 10 similar cases in the literature; in only 1 case was the clinical picture that of involvement of the cord, the symptoms in the other 9 pointing to an intracranial lesion, with remissions in 3.

N. SAVITSKY, New York.

MENINGITIS SEROSA AND RADICULITIS. O. GSELL, Schweiz. Arch. f. Neurol. u. Psychiat. **59**:135, 1947.

The first case is one of polyradiculitis of the Guillain-Barré type in a child. Although nuchal rigidity and a positive Kernig sign appeared to be indicative of meningitis, examination of the spinal fluid disclosed a normal cell count with an increased concentration of protein.

In the second case, a man aged 56, was taken ill with severe headache. During a period of three weeks prior to admission he complained of pains in the chest and finally exhibited facial paralysis. Examination revealed facial diplegia, weakness of the right vocal cord, signs of meningeal irritation and symptoms of intercostal neuralgia. The first specimen of spinal fluid contained 1,000 cells per cubic millimeter and 120 mg. per hundred cubic centimeters of protein. The concentration of protein later rose to 180 mg. per hundred cubic centimeters; three months after onset, when the patient was recovering, the cell count was 90 per cubic millimeter, and the concentration of protein was 72 mg. per hundred cubic centimeters.

In the third case, that of a man aged 35, headache and signs of meningeal irritation appeared after recovery from an acute infection of the upper respiratory tract. He was promptly admitted to the hospital, where ataxia, nystagmus, dysarthria and weakness of both legs with absence of the patellar and achilles reflexes were observed. During the ensuing months the following conditions developed, in the order named: drowsiness, weakness of the left side of the face

of peripheral type, left hemiplegia and aphasia. Six months after his admission, the ataxia had improved, and weakness in the lower limbs had receded until only the muscles of the thighs remained weak. Papilledema was noted about this time. The patient remained in an apathetic state, and his general condition did not begin to improve until fourteen months had elapsed. The cell count per cubic millimeter of the spinal fluid rose from 181 to 431 during the first month and then fell gradually, to increase again later and reach a maximum of 480. The concentration of protein fluctuated between 120 and 240 mg. per hundred cubic centimeters. More than two years after his admission the cells numbered 67 per cubic millimeter, and the protein concentration was 280 mg. per hundred cubic centimeters. The protein level was still 94 mg. per hundred cubic centimeters thirty-seven months after onset.

The fourth case is that of a child with recurring meningitis, apparently due to chronic tonsillitis. Although signs of meningeal irritation had been noted in four of a long series of febrile illnesses, the spinal fluid was examined on only two occasions; it was normal the first time and contained 10 cells per cubic millimeter on second examination; on the third episode examination revealed nuchal rigidity. During a period of six years following tonsillectomy the child experienced only a few relatively mild acute infections.

The fifth case is that of a man aged 34 who, after early recovery from an attack of acute poliomyelitis with a minimal degree of paralysis in the lower limbs, complained of weakness in the hands. Examination a year later revealed the usual signs of myotonic dystrophy. A sister was known to have cataracts, and the father was operated on for cataract at the age of 60. The belief is expressed that the attack of acute poliomyelitis hastened the onset of myotonic dystrophy.

The last case is that of swineherd meningitis due to Leptospira pomona. The patient, a boy aged 17, had been tending hogs in a region where other cases of the disease had been reported. On admission five days after he was taken ill with headache, high fever, signs of meningeal irritation and changes in the urine indicative of mild nephritis were noted. The spinal fluid was under increased pressure but was otherwise normal; three days later, when the temperature, which had been gradually declining, rose again, the cell count was 252 per cubic millimeter, and tests for globulin gave a positive reaction. The causative organism was recovered on culture from the first specimen of cerebrospinal fluid and an agglutinin titer of 1 to 800 was demonstrated in the blood on the tenth day of the illness. Recovery was complete within two and one-half weeks.

DANIELS, Denver.

PRIMARY SARCOMATOUS MENINGITIS. S. BRONFMAN and M. REUMONT, J belge de neurol. et de psychiat. **47**:729 (Dec.) 1947.

The authors describe 2 cases of primary sarcomatous meningitis, 1 of a child and 1 of an adult, and review the literature on the subject. In spite of the diffuse character of the disease, it is possible to distinguish a spinal variety, with symptoms of compression and interruption of conductivity of spinal pathways; a cerebral form, with symptoms suggestive of intracerebral neoplasm, and a type with manifestations of either polyneuritis or polyradiculoneuritis. The changes in the cerebrospinal fluid are characteristic; the fluid is xanthochromic, with a striking increase in protein; the sugar content is decreased, and the cell content is normal at the onset, but there is a rapidly increasing pleocytosis. The disease is rapidly progressive, and the duration rarely exceeds five months.

DEJONG, Ann Arbor, Mich.

Diseases of the Brain

INVOLVEMENT OF THE NERVOUS SYSTEM BY MALIGNANT LYMPHOMA. H. J. SPARLING, R. D. ADAMS and F. PARKER, Medicine **26**:285 (Sept.) 1947.

Sparling, Adams and Parker present a classification of the malignant lymphomas involving the central nervous system based on the histologic characteristics of the principal cell type of the tumor. The special cells of the lymph node—the mature lymphocyte, the lymphoblast, the plasma cell and the reticulum cell—are each capable of undergoing neoplastic transformation. The tumor reproduces more or less faithfully the cells from which it is derived. The authors describe the histologic characteristics of each of the lymphomas and the pathologic changes in the nervous system observed at autopsy in 118 cases. Since lymphoid tissue is not a normal constituent of the brain or spinal cord, the types of lymphoma derived from lymphocytes, lymphoblasts and plasma cells do not arise within the brain. The tumors derived from histiocytes, Hodgkin's sarcoma and reticulum cell sarcoma occur as primary tumors of the brain; 3 cases of each of these varieties are recorded in the present series. In none of the cases was there a proved solitary lesion in the spinal epidural space. Secondary involvement of the nervous system is usually the result of extension from a nearby tumor; metastasis is infrequent. Involvement of the intracranial dura is usually the result of invasion of tumor through the bones of the base of the skull from lymphomatous masses in the pharynx or cervical lymph nodes. The spinal epidural space may be invaded by extension from retroperitoneal, mediastinal or cervical masses or by extension of tumors extension through the base of the skull of lymphoma in the pharynx or the invading of the vertebrae.

The clinical syndromes of lymphomatous disease of the nervous system are the manifestations of acute or subacute compression of the spinal cord; successive implication of cranial nerves, or, rarely, of the cerebral cortex; meningeal invasion by the lymphoma, with or without implication of the cranial or spinal nerves or cerebral invasion, and/or rapidly developing cerebral symptoms.

FRANKEL, Philadelphia.

CEREBRAL HEMORRHAGE FOLLOWING REPAIR OF A COMMON CAROTID–INTERNAL JUGULAR ARTERIOVENOUS FISTULA. A. O. SINGLETON and A. O. SINGLETON JR., Surgery **23**:75 (Jan.) 1948.

Singleton and Singleton report on the operative treatment of a man aged 49 who had an arteriovenous fistula between the second division of the common carotid artery and the internal jugular vein on the left side. The jugular vein was ligated proximal and distal to the fistula, and the arterial opening was closed through the venous opening. A pulse was felt immediately in the carotid artery distal to the fistula and in the corresponding temporal artery. Although the patient was in good condition immediately after operation, he could not be aroused four and one-half hours later, and he died six and one-fourth hours later. Postmortem examination revealed a hemorrhage from the left lenticulostriate artery with a large intracerebral blood clot in the left temporoparietal region and rupture into the ventricular system and into the subarachnoid space. The authors assume that the lenticulostriate artery, although normal anatomically, was unable to withstand the added load placed on it when the internal carotid artery was restored.

FRANKEL, Philadelphia.

SYNDROME OF INTRACRANIAL HYPOTENSION ACCOMPANYING INSULIN COMA: EFFICACY OF CEREBRAL PNEUMOTHERAPY. J. DELAY, P. PUECH, G. VERDEAUX and S. BRION, Encéphale **37**:261, 1948.

Delay and Sizaret recently discussed the problems of intracranial hypotension and the use of insufflations of air into the ventricles to combat the hypotension. In the present paper, the authors describe a case of intraventricular hypotension occurring in the course of insulin shock treatment which was cured by injections of air into the ventricles.

The case was that of a 32 year old woman with catatonia who was placed in insulin coma for the fourth time by intravenous injection of 85 units of insulin. After one hour of deep coma, the usual attempt was made to terminate it by injection of 33 per cent dextrose intravenously. After administration of 250 cc. of the solution the patient could not be aroused from her coma. Immediately after the injection of dextrose, a chronic contraction in extension, with pronation of the arms, occurred. The coma persisted, but the contraction disappeared after one or two minutes. Then occurred a generalized grand mal type of seizure. Two injections of hypertonic sodium chloride solution and serum, together with 20 cc. of dextrose, merely exaggerated the symptoms. Each injection of fluid seemed to release a new epileptic attack. The original belief that the symptoms were the result of cerebral edema was altered. It was thought possible that the patient had an intraventricular collapse. The pulse rose to 130 and the temperature to 39.1 C. (102.4 F.). A neurosurgeon confirmed the opinion that the case was one of hypotension, and surgical intervention was decided. The dura mater on both sides was found to be retracted and hypotensive. The ventricles were punctured bilaterally; very little liquid flowed out, and that which did come out was slightly rose tinged. Air was injected freely and easily; about 20 cc. was injected into the right ventricle. The brain seemed to be slightly inflated. The brain as exposed on both sides appeared edematous and gelatinous in spite of the hypotension. After insufflation of the ventricles, the epileptic phenomena ceased immediately and definitely. The following day the patient still did not respond to questions and showed generalized hypertonia with absence of tendon and abdominal reflexes and of responses to plantar stimulation. The fundi appeared normal; the right corneal reflex was absent, the pulse rate was 120; the respiration rate, 25 to 30, and the temperature, 38 C. (100.4 F.). Forty-eight hours after operation the patient was out of coma, and the mental state seemed improved, although far from normal. Her initial mutism had disappeared; she was loquacious and revealed many paranoid ideas.

The authors note, as did Sakel, that late convulsions appearing during coma carry a grave prognosis and often have no relation to the degree of hypoglycemia. The authors also call attention to two important signs: (1) decreased circulation with reddish edema of the limbs and generalized cutaneous edema in spite of a normal blood pressure, and (2) absence of classically increased spinal fluid pressure, as well as of intracranial hemorrhages. The whole picture seems to be one of a somewhat accentuated ventricular hypotension. Delay and Moreau in 1944 noted that the curve of the depth of coma followed the variations in intracranial pressure. Edema and ventricular collapse are the positive and negative aspects of the same phenomenon observed during the course of hypoglycemic coma and are related to disturbances in the hypothalamic center. The diagnosis of ventricular hypotension must be suspected on the appearance of repeated convulsive episodes—above all, when such episodes are released and repeated after intravenous injections of hypertonic dextrose solution. Only ventricular puncture can definitely indicate whether hypotension is present. Lumbar puncture may be dangerous and/or erroneous. The medical treatment should consist in establishing a rapid increase of blood sugar, all use of hypertonic solutions of any kind being avoided, and rehydration by admin-

istration of isotonic solutions, the vitamin B complex, epinephrine and strychnine. If this treatment fails to arouse the patient, surgical intervention, consisting of intraventricular puncture and injections of air may be necessary.

ZINKIN, New York.

Diseases of the Spinal Cord

CAUSATION AND TREATMENT OF PAINFUL STIFF SHOULDER: SUBDELTOID BURSITIS, PERIARTHRITIS, TENDINITIS AND ADHESIVE CAPSULITIS. HENRY W. MEYERDING and JOHN C. IVINS, Arch. Surg. **56**:693 (June) 1948.

Meyerding and Ivins analyzed 150 cases of painful stiff shoulder. The condition was more prevalent in women (65 per cent) than in men. A history of trauma was obtained in 54 per cent and of antecedent systemic infection in 65 per cent. In most cases (72 per cent) the cause remained obscure; the onset was gradual and the course intermittent. Thirty-nine per cent of roentgenograms showed abnormal calcifications in the shoulder, and 23 per cent, osteoporosis. In the remainder of the cases, the roentgenograms revealed nothing abnormal.

Painful stiff shoulder may be caused by degenerative, often calcifying, lesions in the rotator cuff of the shoulder, which is formed by the tendons of the teres minor, supraspinatus and infraspinatus and suprascapularis muscles. The subdeltoid bursa and the acromial bursa are not the primary sites of the lesion, although they may become secondarily affected. The changes may be associated with adhesive bursitis and synovitis of the shoulder joint. In the differential diagnosis, one must consider the following conditions: tuberculosis of the shoulder joint and bursa, acromioclavicular separation, fractures of the humerus and glenoid cavity, rupture of the supraspinatus tendon and neoplasms of the shoulder.

Treatment may relieve the pain, but not always the stiffness. In the acute and subacute stages, conservative management is indicated (diathermy, physical therapy and roentgen therapy). In the more advanced, chronic stages, manipulation and surgical treatment may become necessary. Satisfactory functional results were obtained by such measures in 85 per cent of the cases under consideration.

LIST, Grand Rapids, Mich.

ATYPICAL NEURALGIA OF THE FACE. A. SZUJEWSKI, Arch. Surg. **56**:785 (June) 1948.

Atypical facial neuralgia may be of vascular origin, the result of irritation of the adventitial sympathetic plexus of the carotid artery. This condition may be caused by inflammatory changes in the lymph nodes surrounding the large vessels of the neck. Periarterial stripping of the artery and its branches achieved a cure in 3 reported cases; however, in 1 instance temporary hypertension of the carotid sinus was produced.

LIST, Grand Rapids, Mich.

COMPRESSION OF THE SPINAL CORD CAUSED BY HODGKIN'S DISEASE. M. J. SMITH and K. W. STENSTROM, Radiology **51**:77 (July) 1948.

Smith and Stenstrom report 11 cases of compression of the spinal cord due to Hodgkin's disease. In 8 cases operation or autopsy confirmed the presence of an epidural mass. Sharp, lancinating backache was the commonest and earliest complaint. Eventually the neurologic findings were characteristic of compression of the cord. In only 5 cases was there roentgenologic evidence of bony change. Myelograms revealed a spinal block in 3 cases.

Roentgen ray therapy was always used, but when acute compression of the spinal cord was apparent laminectomy and resection of the tumor were performed (7

cases). Radiation therapy consisted of 1,200 r delivered to each of three fields. One of the patients is alive and well over ten years after treatment, while 3 others are alive and well at the time of writing, for periods up to fourteen months. Of the 7 others who died, 2 lived approximately four years.

The authors believe that intensive roentgen therapy to the cord of a patient with Hodgkin's in the pain stage will prevent paraplegia. When symptoms of compression are severer, immediate laminectomy should be performed. In these cases radiation therapy alone is of no lasting value.

TEPLICK, Philadelphia.

LARYNGEAL PARALYSIS ASSOCIATED WITH CARDIAC HYPERTROPHY. F. T. LAND, Brit. M. J. **2**:1018 (Dec. 11) 1948.

Land reports 4 cases of laryngeal paralysis attributable to a coexisting cardiac lesion, a condition which he believes occurs more often than is suggested by the scarcity of recorded cases. The most plausible explanation of the symptom has been proposed by King, Hitzig and Fishberg. They stated the belief that compression of the nerve against the arch of the aorta and the ligamentum arteriosum is due to dilatation of the pulmonary artery produced by engorgement of the lesser circulation. They concluded that the hypertension in the lesser circulation is an important factor in the production of laryngeal paralysis complicating mitral lesions.

ECHOLS, New Orleans.

POLIOMYELITIS: EFFECT OF EXERTION DURING THE PRE-PARALYTIC STAGE. E. R. HARGREAVES, Brit. M. J. **2**:1021 (Dec. 11) 1948.

An analysis of 30 cases of poliomyelitis which occurred in Cornwall County, England, during 1947 and 1948 was made by Hargreaves in an effort to determine the effect on the ultimate prognosis of physical or mental exertion during the preparalytic stage of the disease. In agreement with a previous report by W. R. Russell in 1947, the present analysis revealed that severe physical activity during the preparalytic stage was associated with a grave prognosis, whereas only slight paralysis tended to develop in patients confined to bed during the preparalytic stage.

ECHOLS, New Orleans.

CAUSALGIA FOLLOWING SPINAL CONCUSSION. J. PATRIKIOS, Rev. neurol. **79**:649 (Oct.-Nov.) 1947.

Patrikios reports the case of a soldier who after a chest wound at the level of the eighth thoracic vertebra exhibited signs of a transverse lesion of the cord. These cleared in subsequent weeks except for minor signs indicative of a permanent lesion in the spinothalamic and pyramidal tracts controlling lumbosacral dermatomes below the site of the lesion. Concomitant with the patient's recovery of motor power and sphincter control, intense causalgic pains developed in his legs, with extensive trophic disturbances (hyperkeratosis, hypertrichosis and changes in the toe nails), continued suppression of sweating and absence of vasomotor changes. Causalgic pain could be set off as usual by external stimuli to the skin; emotions and noises and were accompanied with considerable psychic changes. The pains were considerably improved with procaine block of the lumbar sympathetic fibers. The patient made a good recovery over a period of five years.

The author reviews theories of causalgic pain and favors the view (1) that most fibers for pain and temperature sensation travel in the sympathetic chain before reaching the cord via the posterior root and (2) that causalgia is due to change in the character of a nerve impulse passing through the site of a partial focal lesion, either peripheral or central, of fibers for pain and temperature sensibility. He feels that normal sensory impulses in crossing such a focus irritate it

and are transformed into abnormally sharp impulses. In this manner he explains the occasionally good result, as in this case, of blocking pain pathways peripheral to the lesion.

LEGAULT, Washington, D. C.

GUILLAIN-BARRÉ SYNDROME FOLLOWING VACCINATION AGAINST SMALLPOX: REPORT OF A CASE. T. LINDQVIST and NILS-MAGNUS STENSTROM, Acta psychiat. et neurol. **23**:278, 1948.

Lindqvist and Stenstrom report a case of the Guillain-Barré syndrome which appeared on the thirteenth day after vaccination.

ALPERS, Philadelphia.

Peripheral and Cranial Nerves

OBSERVATIONS ON THE CAUSE AND MECHANISM OF SYMPTOM-PRODUCTION IN SCIATICA AND LOW-BACK PAIN. M. A. FALCONER, M. MCGEORGE and A. C. BEGG, J. Neurol., Neurosurg. & Psychiat. **11**:13 (Feb.) 1948.

In order to determine the etiology and mechanism of the symptoms of sciatica and low back pain, Falconer and his associates studied two series of cases of the first, or "surgical," group, comprising 100 patients who recovered after removal of prolapsed disks; myelography confirmed the diagnosis in 88 per cent. Of the second, or "medical," group, consisting of 76 patients treated by means of complete bed rest, myelography gave positive evidence in 88 per cent. Thus, while other factors may occasionally be responsible, prolapses of the disk are almost universal occurrences in cases of sciatica and low back pain. A negative myelogram does not necessarily exclude a lesion of the disk. The spontaneous disappearance of the symptoms is frequently associated with persistence of the prolapsed disk. Moreover, the latter may be present without symptoms and frequently exists long before the symptoms arise. This tends to support the contention that a preexisting degenerated disk is of primary importance and that trauma merely acts as a precipitating factor.

With regard to the mechanism of production of symptoms, sciatica and low back pain are to be considered two separate conditions. With sciatica, the prolapsed disk is so situated that it impinges on either the fifth lumbar or the first sacral nerve root in its extrathecal course. Direct stimulation of the nerve root reproduces the symptoms. The root appears stretched over the prolapsed disk, and is occasionally swollen and congested, and the pathologic changes in the sciatic nerve are usually those of edema. Slight blocking in the conduction of impulses through the compressed segment of root would account for the mild signs of muscular weakness, sensory impairment and diminution of ankle jerk usually observed in cases of sciatica. Occasional complete blocking leads to symptoms of foot drop or paralysis arising from lesions of the cauda equina. Exacerbation of the symptoms by coughing or sneezing is characteristic of all root pains. The rigidity and flattening of the lumbar portion of the spine is a protective reflex mechanism. Limitation of straight-leg raising is due to tension produced within the nerve root by predominantly angulation strains resulting from the prolapsed disk. As the symptoms of sciatica wear off, the nerve root elongates and slackens, and this accounts for the recovery better than the protrusion of the disk which frequently persists.

Low back pain, on the other hand, is due to prolapse of the disk itself, presumably through implication of the sinuvertebral nerve of Luschka.

In the opinion of the authors, conservative measures in the form of complete bed rest for at least four weeks should first be tried in the treatment of intractable sciatica or low back pain. Only when this fails should surgical measures be resorted to.

N. MALAMUD, San Francisco.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Benjamin Boshes, M.D., *Vice President, in the Chair*
Regular Meeting, Oct. 14, 1947

Torulosis of the Brain. Dr. John Martin and Dr. Frank Padberg.

A man aged 28 was admitted to the Veterans Administration Hospital, Hines, Ill., on Nov. 23, 1946. He gave a history of head injury in October, followed in two weeks by intermittent numbness of the right arm and leg, with subsequent development of severe headaches, blurring of vision and nuchal rigidity. Examination revealed bilateral papilledema, dilatation of the left pupil, weakness of the right side of the face and the right arm and leg and absence of abdominal reflexes. The spinal fluid contained 2 polymorphonuclear leukocytes and 30 lymphocytes per cubic millimeter. Diagnostic burr holes placed on December 24 for a subdural hematoma demonstrated a softened and purple cerebral cortex of the left hemisphere. Torula histolytica organisms were found in the spinal fluid on December 2. There developed paralysis of the right arm, left arm and right leg; the patient become blind and died on December 30.

Section of the brain showd large areas of softening extending into the white matter under each burr hole. Microscopic examination showed numerous torulas in those necrotic areas. About small foci there were no reactive changes. Torulas were seen within giant cells in sections from the lungs, kidneys and meninges.

DISCUSSION

Dr. George B. Hassin: It should be emphasized that the clinical picture of torulosis of the brain is usually that of a brain tumor. As a matter of fact, in the majority of cases of torulosis of the central nervous system, including my 2 cases, operation has been performed. In 1 of my cases the lesion proved grossly to be a real tumor of the cerebellum, but it consisted of torulas. As to the torular fungus, its shape and size depend on the staining methods used. The authors used Kernohan's stain, a combination of the Bodian and Best methods. In tissue sections the torulas appear as round or oval nuclei with a double membrane. When the organism is stained with toluidine blue, thionin, methyl blue and eosin or methylene blue, a capsule possessing spikes, spines or spicules can be seen. Hematoxylin and eosin or the Van Gieson stain does not show these formations. Some observers, who evidently did not use the proper stains, thought proper to consider these features of the capsule artefacts.

I should like to ask whether the authors saw the soapsuds-like foci. These are not seen in toluidine blue specimens but are seen in sections stained with hematoxylin and eosin or with the Van Gieson method. Time does not permit consideration of other problems in connection with the interesting topic presented.

Dr. Richard B. Richter: I should like to ask whether the impression obtained from the photographs of the gross specimen is the correct one. In other words, are not the large foci of necrosis of cortex and subcortical white matter in a sense artefacts, in that they appear to lie beneath the burr holes placed in the

skull? It would seem that they were produced by the subsequent herniation of the brain into these openings. They do not belong to the picture of the natural pathology of torula encephalitis.

DR. FRANK PADBERG: The "soap bubble" appearance pertained particularly to the large foci in the meninges. We did not attempt to stain any of the specimens with toluidine blue. These large areas of involvement of the white matter were beneath the burr holes in each case. The accumulation of exudate seen on the cortex at the time of removal of the brain actually protruded through the burr holes.

I do not think any definite statement can be given as to how often the organisms are found in the spinal fluid. It is stated that in some cases they are found in the spinal fluid only when looked for; certainly, in the 4 cases of isolated tumors that have been described, these organisms were not found in the spinal fluid and were frequently seen in meningeal lesions. The connection between the accident and the infection is open to debate. In 2 other cases there was a somewhat similar history of preceding head injury, but whether accidents produce changes of this nature is a question.

Aneurysm of the Terminal Portion of the Anterior Cerebral Artery. DR. OSCAR SUGAR and DR. MILTON TINSLEY.

This paper was published in full in the July 1948 issue of the ARCHIVES, page 81.

DISCUSSION

DR. OSCAR SUGAR: Someone has asked how we account for the flaccid paralysis of the arm on the third day. We attributed this to the shock which occurs after a vascular insult of this kind. Almost every spastic paralysis is preceded by a period of flaccidity, attributable to shock.

As to the dangers of this angiographic method, we have had 1 case in which there was laryngeal edema due to infiltration of iodopyracet (diodrast®), and a tracheotomy was performed. This edema is the only untoward effect which we have noted. Occasionally there is contrast medium in the cervical region, but this does not seem to cause annoyance.

DR. MILTON TINSLEY: A patient admitted with a subarachnoid hemorrhage is an emergency. The old idea was to wait and watch the patient for a variable period. It was said that if the patient survived three weeks the chance of recurrence was about 50 per cent. However, the incidence of recurrence over a period of time is 80 or 85 per cent. I would advocate that when angiographic examination can be done one should not wait too long in attacking an aneurysm, because in waiting for three weeks the patient may die or have another episode. We were fortunate that this patient recovered after the second attack, so that an angiogram could be made. If the aneurysm is seen, one can ligate the internal carotid artery or attempt to cut off the aneurysm soon after the angiogram is made.

Threshold Studies in Electrical Convulsions with Use of a Square Wave Stimulator. DR. ALEX J. ARIEFF.

A constant current repetitive square wave (Arieff-Fizzell) stimulator was devised and constructed giving stimuli and intervals from 0.2 to 30 milliseconds. The peak current may be present and kept constant during the convulsion.

For 46 animals, receiving 528 convulsions, the threshold peak current was determined for the various combinations of stimuli and intervals. The optimal duration of stimulation using a minimal current was found to be between 0.5 and

approximately 5 milliseconds. The threshold increased when the stimulus was either increased or decreased.

For all stimuli, there is an optimal duration of interval which is between 33 and 5 milliseconds. Facilitation or summation is evidently maximal at these intervals. The energy with the Arieff-Fizzell stimulator for a convulsion in human subjects is at least one eighth that used in the conventional alternating current stimulator. Convulsive thresholds are minimal, with no or minimal amnesia. The convulsion thresholds are not a function of frequency, as in an alternating current stimulator. The total time necessary to produce a convulsion may be cut to less than one third, with less than twice an increase in threshold.

DISCUSSION

DR. CLARENCE NEYMANN: I should like to ask whether a cathode ray oscillogram was taken while these currents were being applied. It is impossible to tell the amount of current by any other method. The time element of less than a second precludes measurement by a voltmeter or an ammeter. Current is the product of voltage times amperage divided by resistance. If the voltage is increased the current is increased just as the amperage is increased.

DR. S. H. KRAINES: I have had some unfortunate experiences in the treatment of patients with the square wave type of electric current. In attempting to give the minimum possible current, I found that, as with the alternating current apparatus for shock treatment, it was often necessary immediately to increase the voltage or the duration in order to obtain a grand mal convulsion. With the alternating current apparatus the patient does not recall the petit mal reactions, whereas with the square wave apparatus he retains a distinct and vivid recollection of the abortive seizures. After awakening from the grand mal convulsion induced with the square wave current, a patient will state that the abortive seizures which preceded the grand mal attack were like being hit with a hammer or like "a bolt of lightning going through my head." This memory has been so disturbing that many patients have refused to have further shock treatments. When voltage and time factors were so regulated as to make certain that a convulsion occurred, memory loss in several of my patients was as great as that found with the conventional apparatus.

One institution, in an attempt to overcome the possibility of recollection of the "bolt of lightning," used the square wave apparatus on their patients with the alternating current machine set up and ready to be used immediately after an abortive attempt, in order to produce amnesia.

DR. ALEX J. ARIEFF: In reply to Dr. Neymann, this machine has been calibrated with an oscilloscope. Oscillograms have been taken, but not at the time the convulsion occurs. All that the oscillogram would show is a change in the wave form with respect to voltage; it would not show change in the current. That has been brought out by Conrad, Haggard and Teare (*Elec. Engineering Tr.* **57**:1, 1938), who studied passage of current through tissues. There is a change in the load or resistance of the tissue.

In the constant current apparatus a potential of 500 volts is there for use if necessary. One may use more energy (current expressed volts, but not in coulombs, which is measured only in current times seconds). I do not say one does not use more voltage. If the resistance changes, the voltage has to change so that the current can remain constant; the resistance and voltage change, not the current.

Dr. Kraines' inquiry will have to be answered by more work by investigators who are using this type of unidirectional apparatus. With this current, one can

get closer to producing a jacksonian fit without memory defects. Two factors are produced in a convulsion, the motor and the memory pattern. If the strength of stimulation is threshold only, the patient will remember the attack. The strength of stimulation must be increased to the point where one knows that the patient will not have a jacksonian fit alone, but will have a convulsion with memory defect. I am sure some will not agree that the memory defect is necessary; further work must be done to show which is of clinical importance—the convulsion or the amnesia.

Animal sections are being run through for pathologic study, and at present we do not know the cerebral damage. Most animals have shown no damage. When death does occur, some animals die of cerebral hemorrhage; other, of complications due to a fractured spine and paraplegia. Rabbits die too easily.

Benjamin Boshes, M.D., *Vice President, in the Chair*
Regular Meeting, Nov. 11, 1947

Meningitis Treated Intracranially with Heparin and Penicillin: Report of a Case. Dr. Joseph Tarkington.

Pneumococcic meningitis in a boy aged 2 years was treated by intraventricular injections of penicillin with heparin. This treatment effected a cure after systemic administration of penicillin and sulfadiazine had given temporary benefit but failed to control the relapse that followed. The adhesions of the subarachnoid space at the base of the brain, producing cerebrospinal fluid block and hydrocephalus, were released surgically, and heparin was instilled to prevent formation of new adhesions. This is the fourth case to be reported in the literature in which heparin was administered in this manner and for this purpose. There was no clinical evidence of harmful effects from the intraventricular use of penicillin.

DISCUSSION

Dr. Benjamin Boshes: Given a case of severe meningitis resistant to intravenous and intramuscular administration of penicillin, would you use the intraventricular or the intrathecal route? Rosenberg reported on 78 patients treated at Great Lakes via the intrathecal route, with no fatalities and no sequelae during the year of follow-up observation.

Dr. Joseph Tarkington: The majority of workers have stated that they prefer the intrathecal route, using the lumbar region, and that this has been effective in most cases. However, it must be remembered that intrathecal injection in the lumbar region means that the drug will not reach the ventricles or the choroid plexuses, thus permitting exacerbations of the disease when the drug is stopped. It is only by the intraventricular route that a bactericidal level of penicillin can be attained in the ventricular system and around the choroid plexuses.

When adhesions form in the spinal subarachnoid space and cause a fluid block, intraventricular injection is the only route.

Clinical Significance of Electroencephalography in Cases of Cerebral Paralysis. Dr. M. A. Perlstein and Dr. F. A. Gibbs.

Electroencephalograms were made in 284 consecutive unselected cases of cerebral paralysis, 185 of which were of the spastic type (lesion of the pyramidal tract), 87 of the athetoid type and 12 of rigidity and ataxia (lesion of the extrapyramidal tract). The incidence of convulsions was much greater with the spastic type

(60 per cent) than with the athetoid type (16 per cent). Of the spastic patients, convulsive seizures were commonest in the hemiplegic and least common in the paraplegic type; thus the seizures seemed to be more intimately connected with involvement of the arm than with involvement of the leg. From a study of the electroencephalograms in this group the following conclusions were drawn:

1. Spikes are seen with greater frequency in cases of cerebral paralysis than even in cases of epilepsy.

2. The presence of a very abnormal electroencephalogram occurs more than three and a half times as frequently with the spastic as with the athetoid type (60 and 16 per cent, respectively).

3. Even when there is no history of clinical convulsions, 33 per cent of the spastic and only 10 per cent of the athetoid patients have abnormal electroencephalograms.

4. The finding of a normal electroencephalogram in a case of cerebral paralysis without convulsions weights the evidence 2:1 in favor of the condition being of the athetoid type.

5. The teaching of finger skills to the involved hand of a hemiplegic patient may often result in behavior disturbances, speech difficulties and convulsions. However, when the electroencephalogram is normal, or when there are no spikes in the electroencephalogram from the affected side, training of the involved hand in finger skills may be undertaken without danger of precipitating these difficulties.

6. In a case of cerebral paralysis with convulsions it is necessary first to control the convulsions before embarking on rehabilitative training.

Thus the electroencephalogram is of value in corroborating the diagnosis of a convulsive diathesis and in allowing one to follow the course of treatment. It may indicate the correct diagnosis in those cases in which differentiation of extrapyramidal and pyramidal tract involvement exists. It may localize the lesion, and it may be used as a criterion for training the involved arm or leaving it alone.

DISCUSSION

DR. F. A. GIBBS: To my colleagues and me it has been a great pleasure to work on the technical aspects of this study and to see the practical application that Dr. Perlstein has found for our data. He has not mentioned the fact that he does not place a patient under anticonvulsion medication merely because seizure activity is reported in the electroencephalogram. I hope he will give his point of view on this matter.

DR. L. J. POLLOCK: The correlation of certain electroencephalographic evidence of potential attacks in cases of spastic paralysis as contrasted with paralysis with predominantly athetoid movements is very interesting. The thought occurred to me that it is an opportunity for a study that may be related in a more important way to cerebral function. Postplegic athetosis is, of course, much more likely to occur with lesions of subcortical areas. It is not surprising, then, that one sees more manifestations from attacks that occur from cortical lesions. The cerebral paralyses of childhood, comprise a large group. Would it not be well to correlate the pathologic changes in the brain in relation to cerebral paralysis? Some are due to developmental defects before birth; some, to disease of the mother in the period of gestation; some, to infectious diseases in childhood, and there are many other causes. These factors produce lesions with varying localization in the brain—cortical injury or subcortical injury in some cases; atrophy in others;

demyelinating disease in others. I should like to ask, not whether there are more manifestations of potential attacks in the spastic than in the athetoid type, but whether there has been any correlation of areas with potential changes.

DR. R. P. MACKAY: May I inquire whether Dr. Perlstein's experience coincides with mine to the effect that diphenylhydantoin (dilantin®) is less efficacious for seizures due to organic disease than for so-called idiopathic epilepsy? I have found phenobarbital more satisfactory in cases like those he has presented. Another point: Probably patients who appear to have purely athetoid paralysis, but who show spikes in the electroencephalogram or have clinical seizures, actually have a disturbance of the corticospinal pathways as well.

DR. HERMAN JOSEPHY, Lincoln, Ill.: There seems to be a difference between patients with cerebral paralysis seen in the office or in a general hospital and those committed to an institution for the feebleminded. Among the many inmates with cerebral paralysis at the Lincoln State School and Colony were very few with whom one could "work."

I should like to ask Dr. Gibbs whether it is possible to differentiate by electroencephalography between cases with destructive lesions of the brain and those with malformation. I have tried to do so by clinical examination. However, frequently postmortem findings were surprising; destruction was present where one would have expected malformation, and vice versa.

DR. M. A. PERLSTEIN: Would you give medication to a child with an abnormal electroencephalogram who has never had a convulsion? Dr. Gibbs tells me that they have not found a patient past 16 years of age with spikes in the electroencephalogram who has not had convulsions. The inference is that if a child less than 16 years of age has such an abnormal electroencephalogram he will have convulsions before the age of 16. On this basis one would be justified in advising anticonvulsant medication in the presence of an abnormal electroencephalogram even in the absence of convulsions. However, the alternative explanation of Dr. Gibbs's finding is that the electroencephalogram may change before the child reaches the age of 16. On the basis of this possibility, one is justified in not using anticonvulsant medication unless the child has had a clinical convulsion. By so refraining from treatment, one may test the validity of the first premise, that is, that children with abnormal electroencephalograms will eventually have seizures. As a matter of fact, this occurrence has already been observed in a small group of the cases reported here. Of greater import, however, is the effect of being placed under anticonvulsant therapy on the child who has never had a convulsion; psychologic effect on him and on his parents is bad, since it connotates a bad prognosis. As a result of this emotional upset, it is possible to precipitate convulsions in some children who might otherwise never have them. It has been my policy to tell parents whose children have never had convulsions and who ask "what the electric test shows" that the electroencephalogram is normal, no matter what it shows. Although some of these children might later have convulsions. I feel that in the long run I have done more good in allaying fears than harm in the withholding of anticonvulsant medication.

Dr. Pollock mentioned the need of greater correlation between clinical and anatomic findings. I agree wholeheartedly with him. My greatest difficulty has been in finding neuropathologists to study the brains of children with cerebral palsy. If Dr. Pollock would like to make his excellent facilities available, I should be happy to send him some of these brains for study. I think it is especially important to clarify the diagnosis of "cerebral agenesis" and to differentiate between truly genetic defects of the brain and those which are the result of pre-

natal encephalitis, anoxia or hemorrhage. Prenatal pathologic processes are very different from postnatal ones. Such studies might furnish the answer to Dr. Josephy's question also.

Dr. MacKay has found diphenylhydantoin less effective than phenobarbital in control of convulsions due to organic disease of the brain. This has been my experience; at times, however, mesantoin® (3-methyl-5-phenyl-5-ethyl-hydantoin) will be found more effective than either.

Excessive Hunger as a Symptom of Cerebral Origin. Dr. Walter R. Kirschbaum, Manteno, Wis.

The urge for food intake depends on stimuli from the digestive system to the neurovegetative and metabolic centers of the medulla oblongata, of the midbrain and of the diencephalon, and on stimuli from certain cortical regions. Few of these areas are accurately delineated. Their relation to diagnostic localization is vague because of the multiplicity of endogenous and exogenous psychic and somatic factors which result in remarkable changes in the drive for food. This study, a fraction of the complex problem, deals with the origin of automatisms and the localization of psychomotor reactions involved in morbid hunger or excessive appetite resulting from organic conditions. Overindulgence in food, hyperorexia, though much less frequently observed, is a more significant and specific symptom for a clinicopathologic investigation than the opposite, and more general, occurrence, anorexia.

Excessive hunger of cerebral origin was observed in 30 patients with various organic diseases of the brain. Postmortem observations, previous case reports and studies of the literature on animal experiments allowed classification of the material according to the special cerebral structures involved. Diseases of the other systems being ruled out, the following conclusions were reached:

It is reasonably safe to state that cortical or subcortical frontal, as well as hypothalamic, disturbances are instrumental in certain changes in food behavior experienced as excessive hunger. This symptom stands on the borderline between true psychic functions and psychosomatic reactions. It is either conspicuous and prominent or only partly uncovered among the variety of psychopathologic phenomena in the diseased mentality of the patient as a whole. Its significance as a release phenomenon is beyond doubt. It may combine, as the various frontal lobe processes show, with the hypokinetic-apathetic or with the hyperkinetic-hypomanic restless type of the frontal lobe syndrome. Not infrequently it appears with an amnestic, confabulatory mental disturbance. It is likely to arise with alterations of orbital mesiofrontal and basal areas converging on the diencephalon and the mesencephalon, as indicated by several cases with additional damage to the olfactory tracts and the anterior cerebral fossa. Its independence of the precentral corticomotor pathways is as noteworthy as its lack of regular correlation with disturbances of other autonomic functions controlled by frontocortical centers, e. g., micturition. The symptom is likely to originate from a bilateral disturbance of the respective frontal and axial areas. It may initiate a disease of the frontal portion of the brain, and thus it deserves more attention as a local sign. In general, it is transient and reversible, occurring as a "separate" symptom with lesions of the frontal lobe and as a "combined" symptom with other vegetative and metabolic changes in diencephalic processes.

It remains to be investigated whether or not the symptom of excessive hunger is a response to primary involvement of gastrointestinal autonomic centers in the

frontal lobes and the diencephalon, or a sequel to gastrointestinal overactivity reflecting on the cerebral centers. Independent of its central or its peripheral origin, excessive hunger is a sensory phenomenon at a lower integration of consciousness. It appears to be a regression pattern of reaction, a preformed mechanism, displayed also in psychoneurotic conditions and functional psychoses.

DISCUSSION

DR. WALTER KIRSCHBAUM, Manteno, Wis.: Dr. Leindorfer discussed the central hyperglycemic action of epinephrine on centers of the diencephalon and frontal lobe, and the possible involvement of these centers in diabetes mellitus after injuries to the brain. Glucose levels of the blood should be studied before and after operations on the frontal lobe.

As changes in carbohydrate metabolism were not shown in these cases of organic disease of the brain, the excessive drive for food cannot be attributed to a hyperglycemic or a hypoglycemic condition. The normal hunger sensation is not associated with changes in the glucose level of the blood. The nutritive substances lack of which accounts for hunger sensations is not known.

The Sacral Innervation of the Human Bladder. DR. ROBERT F. HEIMBURGER.

The sacral nerves were studied in 12 patients with neurogenic bladder. Nine of the patients had extremely hypertonic bladders, and the condition had been treated unsuccessfully with tidal drainage for many months. The functional innervation supplied to the detrusor muscle through each pair of sacral nerves was measured by blocking them with procaine as they emerged from the sacral foramens. Tone of the detrusor muscle was measured by a standardized method of cystometrography. The cystometrogram obtained after the block of each pair of nerves differed from the control studies for each individual patient and from those obtained after bilateral block of the other sacral nerves. The compiled results of this investigation show marked relaxation of the detrusor muscle in 3 of 7 patients after bilateral block of the second sacral nerves and slight relaxation in the remaining 4 patients. Bilateral block of the third sacral nerves in 8 patients produced pronounced relaxation of the detrusor muscle in 7 patients and slight relaxation in the eighth. Of the 7 patients subjected to block of the fourth sacral nerves, 1 showed marked relaxation and 2 slight relaxation, while there was no change in detrusor response in the remaining 4 patients.

The other 3 patients had bladders of normal tonus but had urinary retention when the indwelling catheter was removed. They were subjected to bilateral block of the third sacral nerves after an unsuccessful attempt to void without a catheter. All 3 patients voided immediately after the block was completed. The procedure was repeated several times—in 2 of the patients to relieve retention which followed several days of voluntary micturition. Permanent voluntary control of urination resulted from a month of this treatment. In the third patient retention was relieved on two occasions, but only during the period in which the block was effective. In a few of the patients studied by cystometrograms, sphincter tone could be measured, as urine leaked around the urethral catheter when the intravesicular pressure reached 70 cm. of urine. After block of some of the sacral nerves, leakage occurred around the catheter at an intravesicular pressure of less than 70 cm. This leakage was due to relaxation of the sphincter. After bilateral block of the second sacral nerves in 2 patients, pronounced sphincter relaxation occurred in 1 and slight relaxation in the other. There was marked sphincter

relaxation in 4 of 7 patients after block of the third sacral nerves, and no relaxation in the remaining 3 patients. No sphincter relaxation was present after bilateral block of the fourth sacral nerves in 4 patients.

These data show that the third sacral nerve roots are dominant in supplying innervation to the human detrusor muscles. The second and fourth sacral nerves also contribute, the second more commonly and to a greater extent than the fourth. The data suggest that the third sacral nerve is dominant in control of the sphincters of the bladder, as measured by this method. Review of the literature shows that anatomists who have dissected the bladder in cadavers agree with this distribution of the innervation from the sacral nerve roots to the bladder.

DISCUSSION

DR. L. J. POLLOCK: This study is an important contribution, for there are in various hospitals many patients with residual symptoms of lesions of the spinal cord and cauda equina. Although the anatomy of the bladder has been worked out well, and studies of the sympathetic and parasympathetic nerve supply have been fully described, a peculiar situation in clinical observation has arisen. After World War I, Riddoch, Head, Holmes, Denny-Brown and others laid down the dictum of response of the bladder following complete section of the spinal cord, one of the characteristics of which was inclusion of the automatic bladder with a mass reflex. I was much interested in the study of bladder function among the veterans of World War II at Hines. Much to my surprise, the conditions described following the first world war could not be found in this group. The new antibiotics have permitted these patients to live for longer periods than those reported after World War I, when it was rare to see cases of survival of more than nine, or possibly eighteen, months. In cases of total destruction of the spinal cord I have not been able to find any of the complete mass reflexes—emptying of the bladder and increased sweating below the level of the lesion. From the standpoint of behavior of the bladder, I am unable to note much difference between cases of injury to the spinal cord and those of injury to the cauda equina. In 21 cases of verified complete anatomic section of the cord, not 1 instance of complete mass reflex was found. There were 7 instances of automatic emptying of the bladder without relation to sweating or spasm, 6 of retention, 3 of constant dribbling from an automatic bladder and 2 of intermittent incontinence. Of 7 cases of complete severance of the cauda equina, retention was present in 1, dribbling in 2, automatic bladder with almost complete emptying in 2 and intermittent incontinence in 2.

I was much surprised that in so few cases could facilitation of urination be elicited by various types of stimuli. Results of some types of stimulation were recorded. Drinking cold water sometimes did as well as pounding on the abdominal muscles.

When the spinal cord or cauda equina was resected, an automatic function finally developed. Then, if some other portion of the nervous system was severed, as in rhizotomy, because of severe spasm, the function of the bladder was temporarily modified. Shortly afterward it would return to the original state. Any peripheral postganglionic procedure was quickly followed by return of the previous type of function; this was also true when chordotomy was done at a level above the lesion.

DR. VICTOR E. GONDA: I was interested to hear that interruption of the fourth sacral nerve caused remission of the clonus, and wondered whether it was temporary or permanent. If permanent, the discovery would be a great contribu-

tion to patients who have this undesirable bladder clonus when sitting. It would indeed be of great benefit if, with such a simple procedure, one could make the life of patients with "spastic" bladder more enjoyable.

DR. ROBERT F. HEIMBURGER: I have no explanation for the improvement of bladder function after bilateral block of the third sacral nerves. In 1 case alcohol was used after procaine block had been successful in relieving retention on several occasions. This may explain the enduring result in this case. The remission of spontaneous clonus was observed only once, in 1 patient. It was pronounced for about two hours after bilateral block of the fourth sacral nerves with procaine.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Charles L. Kubik, M.D., *Presiding*

Regular Meeting, April 17, 1947

Disseminated Encephalomyelitis Experimentally Produced by Use of Homologous Antigen. DR. L. RAYMOND MORRISON.

This article was published in full in the October 1947 issue of the ARCHIVES, page 391.

DISCUSSION

DR. LOUIS DIENES: The symptoms of disease as one observes them are caused in large part by the immunity response which is destined to eliminate the disease. A few months ago Dr. Fell showed us moving pictures of the phagocytosis of tubercle bacilli in tissue cultures. The bacilli are taken up by the microphages and fibroblasts, and the cells continue to divide and to grow. They are harmed only when mechanical distortion becomes too great. Conditions are different when cells from tuberculous animals are studied. They are killed in a short time when they are brought into contact with the bacillus. In this situation the cells are injured not by toxins or by the various substances which are usually considered in connection with the pathologic effects of bacteria, but by the changed reactions of the cells. The importance of the immunity response as the cause of the disease symptom was first realized by von Pirquet. Forty years ago he pointed out that serum sickness, which is caused by a protein introduced into the organism, reproduces the essential features of infectious disease. In the case of a short infectious disease, such as vaccinia, the disease symptoms become apparent when the immunity response reaches a certain stage of development. The pathologic changes often have a similar origin. In diseases like syphilis or tuberculosis the type of tissue response is determined by the stage of the development of immunity response. There is a whole group of infectious diseases in which the lesions are closely similar and are due mainly to the immunity response. Experimental study of the role which allergy plays in human diseases remained fruitless for a long time, the reason being that the methods used were ineffective in reproducing in experimental animals the immunity response developing during the disease. Lewis, to whom Dr. Morrison referred, pointed out that during an infectious disease animals respond more strongly to immunologic stimulus than do animals in normal condition. The difference is often striking. The use of adjuvants allows the reproduction in normal animals of the conditions present during infection and gives an efficient tool for study of the effects of the immunity response. Investigations along these

lines are promising, especially in chronic diseases, and they may clear up the origin of certain conditions which have thus far been obscure.

DR. PAUL ZAMECNIK: My comments are related to Clostridium welchii toxin. In 1939 Seifert and Nägler observed a peculiar opalescence of the serum of animals and of human subjects who had severe Cl. welchii infections. A fatty layer appeared to rise to the surface when the serum of these animals was incubated overnight. MacFarlane and Knight (Biochem. J. **35**:384, 1941) extended this observation by identifying the toxic filtrate (alpha toxin) as probably identical with an enzyme. They demonstrated that this alpha toxin was able to split lecithin and liberate phosphorycholine and a diglyceride. Dr. Lipmann and I became interested and studied the specificity of the enzyme. Cl. welchii lecithinase did not hydrolyze cephalin, sphingomyelin or any phosphatide other than lecithin. This lecithinase would appear to be an interesting tool to use in attempting to study experimental demyelination. Dr. Morrison and I studied the effect of injection of Cl. welchii toxins intravenously in animals. We hoped that some toxin might get through the blood-brain barrier, but such was not the case. The animals died of systemic effects of the toxin. The blood was rapidly hemolyzed, and they did not live long enough for demyelination to develop. Smaller doses given repeatedly to animals produced no cerebral effects. It appeared that the blood-brain barrier prevented the toxin from coming into contact with the brain cells. As Dr. Morrison has pointed out, toxin will demyelinate brain if given a chance, either when toxin is injected intracerebrally or when the toxin is incubated in vitro with slices of brain or cord. Dr. Morrison has devised a pretty technic by which the effect of lecithin on myelin may be studied. As phosphorylcholine is split away from lecithin, it may be trapped in situ by having the reaction take place in the presence of calcium, since the calcium salt of phosphorylcholine is insoluble. Addition of lead nitrate results in displacement of calcium by the lead. Now, addition of ammonium sulfide produces a final precipitate of lead sulfide at the site of hydrolysis, where the phosphorylcholine was split away. Thus, one obtains histochemical evidence of the site of action of the toxin.

Twenty Years' Experience in Treatment of Trigeminal Neuralgia. DR. A. M. DOGLIOTTI, Turin, Italy.

Two thousand cases of trigeminal neuralgia treated according to the alcoholization method were reported. In recent cases, especially of young persons, simple alcoholization of the involved peripheral branch is advised; this procedure seems preferable to radical treatment because pain is relieved for a number of months and because the patient becomes aware of the sensory disturbances consequent to the induced anesthesia. In cases of severe and long-standing neuralgia radical operation is felt, instead, to be the method of choice. Of the two kinds of treatment generally accepted, that of alcoholization of the gasserian ganglion or of its posterior root and that of neurotomy, the former seems preferable as applicable to almost all ambulatory patients; it is not practicable only when the ganglion or its posterior root cannot be reached, for anatomic reasons. This occurred in my series in an extremely limited number of cases in which a neurotomy had to be performed. I prefer alcoholization of the posterior root, and the technic I follow is described here: A thin needle, as used for spinal puncture, is introduced through the check into the foramen ovale; once the needle has pentrated Meckel's fossa, the jugular veins of the neck are compressed, and the needle is pushed several millimeters farther, until cerebral fluid is obtained. This proves that the needle is inside the arachnoid sac, which envelops the root of the trigeminus nerve.

At this point, from 0.4 to 0.5 cc. of absolute alcohol is slowly injected with continuous testing of the cutaneous sensibility and the corneal reflexes.

After the injection a deep anesthesia occurs, but in a few hours it disappears to a considerable extent, leaving a few anesthetic and hypesthetic areas here and there. If after two hours the corneal reflexes are still missing, it is necessary to close the eye completely and, this done, to apply a watch glass to it with adhesive tape. This protection must be maintained for from ten to fifteen days. Neuroparalytic keratitis is avoided in this way. In 30 per cent of my cases I obtained complete recovery after a single injection of alcohol. In the remaining cases there was recurrence one to twelve years later. In these cases a second, or, if necessary, a third injection of alcohol was performed, followed by permanent recovery. No fatalities resulted in any of my cases. Keratitis developed in 10 per cent of the cases. Loss of eyesight on the side of operation occurred only in 5 patients, who had not followed the advised precautionary measures.

In the 40 cases in which retrogasserian neurotomy was applied, I followed the technic of Frazier. In 4 cases in which this technic could not be applied, I resorted to an original approach, above the cerebellar tentorium. First, the occipital lobe was raised, and the cerebellar tentorium was cut through about 2 cm. behind the petrous bone, so as to reach the great tentorial incisure. The cerebellum was then pushed aside, and the arachnoidal membrane was lacerated in order to expose the trigeminal roots. After exploring the cerebellopontile angle for new growths or other pathologic processes, the sensory root was incised, avoiding the motor root.

I used this approach in 1935, for the first time, in performing the section of the lemniscus at a level corresponding to the lateral sulcus of the mesencephalon. At this level the sensory fibers of the spinothalamic tract are located rather superficially. By this intervention it is possible to interrupt pain sensibility in all or in part of the opposite half of the body.

DISCUSSION

DR. JAMES L. POPPEN: I enjoyed Dr. Dogliotti's paper, but I must disagree with some of the things mentioned. All who have had experience with tic douloureux know that, although the disease is not a matter of life and death, it is a serious problem for the patient. Tic douloureux will not kill unless the patient kills himself, or unless the condition is secondary, as a result of dehydration. In cases of minor tic douloureux, we are agreed that the simple methods, in the form of medication, should be used. Many medications will take care of the condition temporarily. It is important that the patient does not have any form of surgical treatment until he has been well informed about the nature of the disease and the nature of the treatment that can be instituted. If the physician sees such patients regularly, as Dr. Dogliotti, Dr. Mixter, Dr. J. C. White and others have, he finds that it is not all a bed of roses. There are many heartaches connected with the treatment of trigeminal neuralgia in patients who do not, I believe, have true tic douloureux but some other kind of neuralgia. It is important that the simpler treatments be instituted first, and later more radical surgical measures. I agree with Dr. Dogliotti that it is important, if operation must be performed, that the patient be subjected to temporary anesthesia. Only after the patient has experienced anesthesia for several days, months or years can he decide whether he would prefer anesthesia or pain. It is true that the happiest patients are those who are successfully treated for tic douloureux. Nothing one can do is more satisfying. There is a definite percentage, however, who

make the physician's life miserable. An attempt should be made to educate the patient as to what he must expect; the worst complications are paresthesias, or perverted sensations, which are present in 50 per cent of cases. These sensations may be of itching, crawling, burning, fulness or tightness. If the patient is educated to expect that type of paresthesia and wishes to get rid of the attacks of pain, I believe that operation is indicated.

With respect to alcoholic injection, my colleagues and I have done only peripheral nerve blocks, except in a few cases in which the ganglion was injected. It is true that if one does any procedure often enough, one becomes an expert, as is the case with Dr. Dogliotti. Certainly, I should be fearful of injecting absolute alcohol into the posterior roots. I should be afraid the alcohol might spill into the posterior fossa along the eighth and seventh nerves. Dr. Dogliotti is an expert at this procedure, and evidently it is safe in his hands. I should hesitate to teach the practice of posterior root injection unless the men had served a considerable apprenticeship and had seen a few cases of facial paralyses, or tinnitus which were distressing. Injections of peripheral nerves are usually adequate, even though the results are temporary. Many New England patients are hardy; they let us do the injection and never say a word, and they come back year after year. We have performed about 2,000 injections of peripheral branches, with relief for an average of ten to fourteen months. When the first division of the nerve only is involved, injection of alcohol usually is not very satisfactory in our hands, since it lasts only a few months. Unless the patient has a fairly large supraorbital notch, it is better to avulse the supraorbital nerve; by this means satisfactory anesthesia is obtained for two years. We have done 525 avulsions of the sensory root. There have been 3 deaths. In 1 out of 50 cases there has been temporary drooping of the face, which began on the third or fourth day and cleared up during the first three weeks. In 2 cases it lasted three months. In all cases, a reasonably normal function returned. We believe that keratitis is of purely traumatic origin. If complete avulsion of the sensory root is done, a small external canthorrhaphy is carried out at the time of operation.

As Dr. Dogliotti mentioned, it is important to instruct these patients as to the care of the eyes. It is well for them to wear glasses and some sort of a shield on the side if they work outside. Avulsions of the sensory root may be followed by annoying paresthesias. Before such an avulsion is performed, we tell the patient the worst about paresthesias and warn him that if he has them he must accept them. Otherwise, he worries lest the tic recur, or he worries constantly about the face.

As to the supratemporal approach, any operation that is performed should be as simple as possible. I do not believe that a simple operation should be made a major one. The approach described by Dr. Dogliotti, in which the veins of Labbé must be occluded, is interesting. I should think that cerebral edema would be frequent and would cause trauma to the cortex. Convulsions might occur. Avulsion of the sensory root by the Frazier-Peet technic is less difficult and less time consuming, taking from eight to forty-five minutes; certainly formation of a bone flap of the type described would take considerably longer, and there would be more danger of damage to the soft tissues. The method is an ingenious one. I do not believe, however, that it would be practical in the ordinary case.

I enjoyed Dr. Dogliotti's presentation. He has done a great deal for the treatment of tic douloureux.

DR. JAMES C. WHITE: Those of us who have attempted the treatment of trigeminal neuralgia by injection of the gasserian ganglion itself have been

impressed by the difficulties of inserting a needle through the foramen ovale into the ganglion, either by the lateral approach described by Wilfred Harris, of England, or by the method of Hartel, in which the needle is inserted upward through the cheek. Dr. Tracy J. Putnam, in the early thirties, while he was at the Massachusetts General Hospital, tried Hartel's technic on a number of occasions, with the aid of roentgenologic control. This method also proved not to be easy, and a number of complications followed its use. If Professor Dogliotti could teach us surgeons, who usually prefer the operative approach, to do successful injections through the foramen ovale in the occasional case of desperate risk or in the case in which it is wished to inject the ganglion for diagnostic purposes, it would be of the greatest value. I hope to be able to go to Italy in the near future and see him perform this operation at first hand in Turin. The method appeals to me particularly for diagnosis in the atypical case of trigeminal neuralgia or in some cases of very severe migraine.

Dr. Poppen has given a complete summary of American operative methods. I should like to reemphasize, however, the extreme importance of accurate diagnosis of trigeminal neuralgia before operation for tic douloureux is considered. This is because in the atypical case the condition is often made much worse if operation is undertaken. I have in mind a patient who had a preliminary infection of her antrum and mild osteomyelitis. This had given her a steady, aching, miserable pain in her cheek. To test out whether partial gasserian root section could help her, I was fortunate enough to produce very complete anesthesia of the second division by injection of alcohol. This, however, had no effect on her pain; so I told her never to let a surgeon cut the posterior root. Nevertheless, her pain was so incapacitating that the root was finally cut. In the intervening years her pain has continued to be just as bad as ever. Fortunately for her, it has not actually made the matter worse by giving her a painful or disagreeable anesthesia, and she is bearing up under her misfortune with considerable fortitude. In all my cases of trigeminal neuralgia I have used preliminary injection of alcohol in nearly every instance. In this way, one can show the patient exactly what surgery will accomplish and what the anesthesia, which will be permanent, will be like. Before operating on any patient for pain, the surgeon should tell him exactly what changes denervation will produce and what he has to go through in the way of risk to achieve relief. Only the patient knows how severe his pain is and what he is willing to pay in the way of permanent anesthesia and risk of complication for his relief.

I should like to comment on the use of retrogasserian neurectomy for pain associated with cancer of the tongue and jaw. In these conditions the pain often involves the glossopharyngeal nerve and the upper cervical roots, in addition to the trigeminal nerve; yet section of all these structures may not give successful relief. Section of the spinothalamic tract in the midbrain, as originally suggested by Professor Dogliotti and further developed in this country by Dr. A. Earl Walker, is, I believe, capable of relieving this pain, but at the risk of a high mortality rate in these patients. Dr. William Sweet and I are now evaluating this procedure and comparing its effectiveness with that of prefrontal leukotomy in this desperate group of patients with advanced and depleting malignant disease.

Dr. William H. Sweet: I should like to congratulate Dr. Dogliotti on his paper and to ask him whether distressing paresthesias are experienced after injection of alcohol into the posterior root. The Harris technic of injection of the ganglion has resulted in paresthesias of the same type as those which follow

operative division of the trigeminal roots. I wonder whether the method of preserving the function of some fibers by using small amounts of alcohol has helped to eliminate the paresthesias.

DR. C. G. TEDESCHI: There is a great disproportion between the considerable investigation done on the treatment of trigeminal neuralgia, and the very little known of the etiology and underlying pathology. Intrinsic and extrinsic factors have been advocated. Among the intrinsic factors, degenerative changes in nerve cells and fibers of the gasserian ganglion were described in a number of cases. In other cases inflammatory changes were observed, and in still others proliferation of fibrous connective tissue was seen to obliterate to a considerable extent the normal ganglionic structure. In Dandy's series, a neoplastic growth was detected in 5 per cent of the cases; isolated reports in the literature seem to confirm the possibility that a new growth may be the cause of trigeminal neuralgia. In my life experience, I have had opportunity in 4 cases to study small pieces of ganglionic tissue removed at the operation: In 2 cases moderate infiltration with lymphocytic cells was present; in the third the blood vessels displayed thickening of the walls and narrowing of the lumens, and, in the fourth there was striking proliferation of fibrous connective tissue. May I add that I noted occasionally a similar sclerotic change in gasserian ganglia from postmortem material in persons who had never had any trigeminal pain during life.

Among the extrinsic factors, malformations of the fossa of Meckel or of the foramens of exit of the peripheral trigeminal branches have been described, but in an extremely limited number of cases. More frequent seems to be the presence of osteomyelitis or osteoperiostitis of one or the other of the bony structures with which the ganglion is in relation; a number of authors have emphasized such pathologic involvement of the bone, especially in concurrence with inflammatory involvement of the cranial sinuses.

Yet a larger category of cases remains in which no recognizable pathologic change can be found to explain the clinical symptoms. In view of this, and of the intermittent nature of the pains which is characteristic of trigeminal neuralgia, one wonders about the real signifiance of the pathologic changes described, and is inclined to accept the opinion expressed by some investigators that trigeminal neuralgia is due to a dysfunction of the sympathetic nervous system. Another factor that might be considered is virus infection, a hypothesis which might find some justification in the frequent association of trigeminal neuralgia and herpetic manifestations.

As few men can claim more experience than Dr. Dogliotti with trigeminal neuralgia, may I ask him to speak of his pathologic observations at operation?

Any kind of surgical intervention is likely to induce some accidental pathologic change. Injury of nerves at the cerebellopontile angle, hematomas and corneal lesions have been described. May I ask Dr. Dogliotti which of the two procedures most frequently used in the surgical treatment of trigeminal neuralgia, namely, alcoholization of the gasserian ganglion and retrogasserian neurotomy, is, in his experience, less likely to lead to complication?

DR. A. M. DOGLIOTTI, Turin, Italy: May I thank Dr. Poppen and Dr. White for their comments? I agree fundamentally with them that the best method is the one in which the surgeon has the most experience. A surgeon after 100 operations can obtain wonderful results, with a low mortality, but a surgeon beginning his work will have many difficulties in obtaining such a result. Dr. Poppen said that he is not against alcoholization when it is performed by me because I have acquired considerable experience. I, in return, can say to Dr. Poppen that I am not against surgical intervention when the operation is performed by him because

of his great experience. But having acquired experience in both, the alcholization of the ganglion or of the sensory root and surgical resection of the sensory root, I am convinced that alcoholization yields results as good as those of resection, with less danger. There were no fatalities in my series with the procedure of alcoholization. Mortality is low, but some deaths have occurred after surgical intervention, especially when the surgeon did not have considerable experience. I observed some cases of temporary paralysis of the nerves of the cerebellopontile angle in the first year of my experience, when I used to inject too much alcohol, 1 cc.; but now, using only 0.4 to 0.6 cc., I do not observe any more complications of this kind. From the practical standpoint, even if the injected alcohol reaches the posterior fossa, it is already so diluted that it cannot affect any nervous structure.

The injection must be made slowly, and the sensibility of the face and the corneal reflex must be continuously controlled. Cephalalgia is rare and temporary. Moreover, I agree with Dr. Poppen that the supratentorial route is more difficult and dangerous than that of the usual Frazier technic; but, as I said, the supratentorial route must be reserved for the few cases in which the Frazier technic cannot be followed.

Dr. Sweet asked me whether I saw paresthesias after injection of alcohol into the posterior root. In many cases there developed a paresthesia of the type seen after surgical operation, but it has been less frequent and less severe since I have used a smaller amount of alcohol.

I did not understand what Dr. White said about recurrences. As I already mentioned, there were recurrences in my series after the first injection of alcohol, especially after I began to inject a small quantity of alcohol. As pains recurred two or three or more years after, I gave a second or a third injection, always using a small quantity of alcohol. Usually after the second or the third injection I did not have any more recurrences. Very rarely I had to recur to surgical intervention, when the patient himself preferred operation or when I could not reach the ganglion.

In answer to Dr. Tedeschi: I cannot tell him more than he said about the causes and pathology of the processes. In a number of cases a tumor or some other visible pathologic process was found, but in essential neuralgia I could never detect any underlying pathologic condition to explain the pain.

NEW YORK NEUROLOGICAL SOCIETY

Samuel Brock, M.D., *President, in the Chair*
Regular Meeting, Nov. 3, 1947

Presidential Address: Dynamic Mechanisms Underlying Some Forms of Cerebral Dysfunction. Dr. Samuel Brock.

Reexamination of Patient with Visual Agnosia Three Years After Injury: Cinematographic Demonstration. Dr. Alexandra Adler.

Two films were shown to illustrate the course and ultimate outcome of visual agnosia in a young, cooperative, intelligent patient.

DISCUSSION

Dr. Kurt Goldstein: I should like to stress that the patient does not show any improvement, or very little, a result corresponding to the usual findings in patients with this disorder. A patient whose case I published years ago and whom

I observed for more than ten years, did not show any improvement. Patients I have observed who were more severely affected than Dr. Adler's learned many things, and even an occupation in which they could earn money. Despite that, the basic defect did not improve. This point is interesting with respect to the compensation for lost functions.

Observations on "Major" and "Minor" Causalgia. DR. FRANCIS ECHLIN, DR. FREDERICK M. OWENS JR. and DR. WARNER L. WELLS.

This article was published in full in the August 1949 issue of the ARCHIVES, page 183.

DISCUSSION

DR. E. D. FRIEDMAN: In Dr. Echlin's experience, was the predominance of involvement in the median and posterior tibial nerves? What was the percentage of involvement of the other nerves, and in what proportion of the cases did he find osteoporosis?

DR. SAMUEL BROCK: I wonder whether Dr. Echlin would tell us what he thinks is the mechanism of causalgia.

DR. FRANCIS A. ECHLIN: Causalgia was only slightly commoner with lesions of the posterior tibial nerve than with lesions involving the common peroneal nerve. The percentage of cases of causalgia with injury to the median nerve was only slightly higher than those with lesions of the ulnar nerve. Major causalgia was seen in only 2 cases of lesions of the radial nerve, but minor causalgia in the distribution of the radial nerve was not uncommon.

Osteoporosis was present in all our cases with major causalgia. I remember 1 case, however, in which a through and through gunshot wound of both legs had injured both sciatic nerves. There was severe causalgia in one leg, but not in the other. The patient had osteoporosis in both feet. I believe that osteoporosis is nonspecific, although it occurs in almost all cases of causalgia of long duration.

In answer to Dr. Brock's question concerning the mechanism of causalgia, I believe that the explanations of Livingston (Pain Mechanisms, New York, The Macmillan Company, 1944) and Doupe and associates (Doupe, J.; Cullen, C. H., and Chance, G. Q.: *J. Neurol., Neurosurg. & Psychiat.* **7**:33, 1944) are the most acceptable, although some of the pain may originate in the tissues of the distal part of the extremity itself, as Thomas Lewis (Pain, New York, The Macmillan Company, 1942) and Mitchell (Injuries of Nerves and Their Consequences, Philadelphia, J. B. Lippincott and Company, 1872) suggest.

Livingston has postulated that the causalgic state is due to a vicious circle of activity originating in nerve impulses from an injured peripheral nerve, with creation of an abnormal state of activity in the internuncial neuron centers of the spinal gray matter. The activity in the gray matter gives rise to efferent discharges, which are responsible for the abnormal muscle spasms and vasomotor and other changes in the periphery. If the process is allowed to continue, the abnormal activity in the spinal cord may become self sustaining and affect the higher centers in the central nervous system.

In some cases breaking the circle peripherally may not be curative, but in the last war the articles of Mayfield and Devine (*Surg., Gynec. & Obst.* **80**:631, 1945), Speigel and Milowsky (Causalgia, *J. A. M. A.* **127**:9 [Jan. 6] 1945), White (*Am. J. Surg.* **72**:468, 1946) and others have shown conclusively that most cases of severe causalgia can be cured by sympathectomy.

Doupe's theory may explain why this is so. He believes that causalgia is the result of stimulation of sensory fibers by efferent impulses in the sympathetic fibers at the site of the nerve injury in some cases, but possibly at a distal site near the termination of the fibers in others. The theory is based on the demonstration by physiologists that interaction between nerve fibers may occur as the result of injury. Doupe's hypothesis is not incompatible with Livingston's, and the two mechanisms may be operating in the same case. There is one objection to Doupe's theory. Although interaction between nerve fibers can be produced in the laboratory in an injured nerve, as Adrian showed long ago (*Proc. Roy. Soc.*, S. B., London **106**:596, 1930), it is hard to visualize how this interaction would remain sustained for any length of time. Inflammatory reaction and interstitial fibrosis are usually set up at the site of injury, and the fibrosis would be expected to insulate or separate interacting fibers. Actually, this may explain why in many cases of causalgia improvement is gradual.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Samuel Brock, M.D., *President, New York Neurological Society, Presiding*

Joint Meeting, Jan. 13, 1948

Sympathicoblastoma with Metastases, Associated with the Clinical Picture of Cushing's Syndrome: Report of a Case. Dr. Lawrence I. Kaplan (by invitation), Dr. Leon Sokoloff (by invitation), Dr. Frank Murray (by invitation) and Dr. Lewis D. Stevenson.

A 14 year old boy was admitted to the neurologic service of Bellevue Hospital in status epilepticus. For one year he had undergone physical changes consisting in deposition of fat in the face, shoulders, back and abdomen. For several months before admission he complained of muscular weakness, pain in the back, epigastric pain, right supraorbital headache and polydipsia. Physical examination revealed hypertension (blood pressure of 155 systolic and 120 diastolic); mild hypertrichosis over the back; dusky, plethoric skin with an acneform eruption on the face; kyphosis of the upper thoracic portion of the spine, and a small nodule in the conjunctiva of the right upper lid. Laboratory studies revealed mild diabetes with decreased sugar tolerance and moderate resistance to insulin; low creatinine excretion (258 mg. per twenty-four hours); osteoporosis, particularly of the spine, with hypercalcinuria; mild erythrocytosis (5,500,000 red cells), and moderate elevation of the 17-ketosteroids. The combination of clinical and laboratory features was typical of Cushing's syndrome, satisfying Albright's criteria. Sudden death followed an episode of acute intestinal obstruction.

Pathologic study revealed a retroperitoneal sympathicoblastoma in the region of the celiac axis, with secondary tumors in the liver, right adrenal gland, lungs, bronchus to the middle lobe of the right lung, pancreas, thyroid, thymus, lymph nodes, vertebral column, skull bones, dura, conjunctiva and retina (clinical). Crooke's changes were found in the basophil cells of the pituitary gland. Other conditions observed included a large abscess in the lesser peritoneal sac, acute fibrinopurulent peritonitis and slight hyperplasia of the zona fasciculata of the adrenal cortex.

This case is recorded because of the concurrent development of clinically established Cushing's syndrome and a pathologically confirmed sympathicoblastoma

with metastases. The manner of relationship between the neoplasm, one of neuroblastic tissue without hormonal function, and the endocrinopathy, unlikely to be coincidental, cannot be specifically determined on an etiologic basis.

DISCUSSION

DR. MEYER MORTON MELICOW (by invitation): This case is certainly interesting, and I want to congratulate Dr. Kaplan and his group for making so fine a presentation.

A few points about it worry me, and I should like to ask the authors to explain them to me. We have had considerable experience at the Squier Clinic with the adrenogenital and Cushing's syndromes and have concluded that either condition when related to the adrenal gland is usually associated with a disturbance in the cortex. We have also seen lesions of the medulla; there we found two types of growths: The first were nerve tumors which we called sympathicoblastomas or neuroblastomas; they occurred in children and tended to metastasize to the skull, liver, etc. (the Hutchinson and Pepper groups). The second type of tumor was the pheochromocytoma. We never found a true neuroblastoma or sympathicoblastoma productive of an endocrine disturbance.

Along the aorta are colonies or cell rests of adrenocortical and medullary tissue. Disturbances in the cortical rests may be associated with adrenogenital or Cushing's syndrome. The medullary rests may give rise to pheochromocytomas or sympathicoblastomas. The microscopic picture in Dr. Kaplan's case is apparently that of a sympathicoblastoma. It is hard for me to visualize how a nerve tumor could have caused the metabolic disturbance which this boy had. After all, it is just nerve tissue. The history does indicate that there was some osteoporosis of the sella turcica and that small metastases were found in the adrenal gland at autopsy. Is it not possible that we are dealing here with a sympathicoblastoma with multiple metastases and that the metastasis to one of the adrenal glands was the factor connected with the endocrine disturbance? This would make Cushing's disease in this patient an accident resulting from the metastasis. Had such metastasis not occurred, the patient would have had merely a sympathicoblastoma without the Cushing syndrome.

I am merely presenting this as a possibility. Furthermore, the condition of the pituitary gland at autopsy was not described. Cases of Cushing's syndrome have been reported in which the pituitary showed little gross change, yet sections revealed a type of hyalinization known as Crooke's changes. I bring up these points because of the doubt in my mind that a sympathicoblastoma per se is capable of producing a metabolic disturbance (Cushing's disease).

DR. SAMUEL BROCK: Were there any changes in the pituitary gland?

DR. LEWIS D. STEVENSON: The pituitary as I saw it was normal in size and staining properties, except for the basophilic cells, which seemed to be hyalinized. I think I have seen this condition before without anything like Cushing's syndrome (present in this case), yet there was no adenoma of the pituitary gland; the basophilic cells were easy to see with the Heidenhain stain, and they had a sort of homogeneously staining cytoplasm.

As to the metastases in the adrenal glands: They were so small and so microscopic in the section I saw that I do not believe they could have disturbed the function of the adrenal, and I do not believe that they could have had anything to do with this picture. Unless these cells in the pituitary gland mean something more than they seem to mean, the changes are hard to interpret. I should like very much to hear whether anybody has something to say on this subject.

DR. LEO M. DAVIDOFF: Would you interpret these hyaline changes in the basophilic cells as similar to the Crooke cells?

DR. LEWIS D. STEVENSON: That is how they were interpreted by the pathologist.

DR. LEO M. DAVIDOFF: It seems to me that this case may more safely be included in that group in which this syndrome is seen with no endocrine tumors whatever, and the pituitary changes are those which Crooke has described, and the sympathicoblastoma be left out of the etiologic picture. I know of no other case in the literature in which this syndrome has been associated with sympathicoblastoma, and we have just heard evidence that sympathicoblastomas have been seen and are not uncommon tumors without the syndrome. Hence I feel that it would be the part of wisdom to leave the presence of this tumor, which was undoubtedly the cause of this child's death, as an incidental finding in a boy with the Cushing syndrome, related perhaps to the physiologic disturbance of the pituitary gland and secondary adrenal changes.

DR. LAWRENCE I. KAPLAN: I agree with Dr. Davidoff. We made no attempt in presenting this case to offer any confirmed etiologic relation between sympathicoblastoma and Cushing's syndrome. We merely presented a case which we considered to be a typical case of Cushing's syndrome with a typical sympathicoblastoma developing concurrently and thereby possibly related in some previously undescribed manner.

Disturbance of Body Image and Allesthesia. DR. MORTIMER F. SHAPIRO (by invitation), DR. HANS-LUKAS TEUBER (by invitation) and DR. MORRIS B. BENDER.

This paper was published in full, with discussion, in the August 1949 issue of the ARCHIVES, pages 222-235.

The Selection of Psychiatric Cases for Prefrontal Lobotomy. DR. LOTHAR B. KALINOWSKY and DR. JOHN E. SCARFF.

Prefrontal lobotomy if applied to the right type of patient is a valuable means of saving patients from the misery of mental illness. Misconceptions such as the belief that only hopelessly deteriorated schizophrenic patients should be treated by lobotomy are as harmful as is the total rejection of the operation for reasons of principle. The decision for or against prefrontal lobotomy is a difficult one and more serious than any other decision psychiatrists are called upon to make. The selection of suitable cases offers problems quite different from those in shock therapy. In prefrontal lobotomy the selection of cases is not simply a diagnostic problem. The first requirement is that the patient has received adequate treatment with nonsurgical methods. A strict attitude in this respect is necessitated not so much by the danger of the operation, which is negligible with the open surgical approach, but by the postoperative changes of personality which follow lobotomy. The usual psychologic tests give little information about these postoperative changes. Even psychiatric interviews reveal little. It is the interview with the patient's relatives which gives pertinent information. Patients who show an excellent performance in the presence of strangers may use vile language as soon as they are alone with their relatives. One should also not be deceived by a good performance in tasks which are not suitable for showing what must be looked for in these patients. Life situations will show better than test situations that these patients do not function like normal persons. This fact should be freely acknowledged, but it should never be a factor in deciding against the operation in patients who are tormented by neurotic symptoms or psychotic ideas. We have made it

a practice in discussing the operation with relatives to differentiate clearly between what they will see after the operation, and what the procedure will do for the patient. If the patient suffers severely from his symptoms, the physician, will have to advise prefrontal lobotomy even if the outcome may prove unsatisfactory to the relatives. The extent to which patients show the symptoms of this postoperative "encephalopathy" varies greatly and seems to depend largely on the patient's premorbid personality. Unpleasant traits will become magnified after lobotomy, whereas a pleasant well adjusted personality diminishes the threat of postoperative difficulties. The promise that the operation will enable the patient to provide again for his family should never be given, because it will lead to disappointment even in many favorable cases. A job alone should not be the measure for the outcome of prefrontal lobotomy. It is the emotional readjustment of the patient both to himself and to his environment that is really essential.

The largest, although hardly the most successfully treated group, is represented by the schizophrenic patients. In this group, shock therapy, which carries with it hope for a full remission or, at least, arrest of the psychosis, should be adequately applied. Both electric shock and insulin treatment should be applied in each case. If a concise treatment plan is outlined at the onset of the psychosis and followed through without wasting time on the various treatments, the potentialities of shock therapy will be exhausted well before the first year of illness is over. At this time lobotomy can and should be considered. Further delay is unnecessary and dangerous, and it is one of the most regrettable errors to wait until the patient is hopelessly deteriorated. Looking for suitable means to determine the point to which a patient with chronic schizophrenia may still improve after the operation, we decided on a test with electric shock treatments. This prognostic electric shock test helps to disclose whether an unresponsive patient is emotionally empty or whether he is blocked and dominated by psychotic manifestations and also whether incoherent talk represents a productive psychotic manifestation or whether it is the expression of irreversibly disconnected thinking. This test proved to be the most reliable means of determining the prognosis of lobotomy in schizophrenia and with us became a routine procedure in the selection of patients. Patients with the subtypes of schizophrenia are suitable for the operation to varying degrees. Hebephrenic persons are rarely suitable for lobotomy. Patients with catotonic excitement are excellent subjects if they have failed to improve under shock therapy, to which those in the early stage usually respond well. In the group with catotonic stupors our experience is not encouraging. Persons with paranoid schizophrenia represents the group in which the best results can be expected. This is especially true for those in the old age group with paranoid syndromes which have been classified as paraphrenia. Their personality remains well preserved, as it also is in the rare patients with true paranoia. Both groups fail to respond to shock therapies, and for them lobotomy is strongly indicated. Patients with the "affective disorders" of manic-depressive psychoses and pure involutional melancholia respond well to shock therapy and should not be freely accepted for lobotomy. Only the rare persons in whom shock therapy fails are suitable. Most of these have complicating neurotic features, have paranoid symptoms or represent cases of true severe hypochondriasis. They are usually unresponsive to both psychologic and somatic treatment, and lobotomy is strongly indicated. The best results are obtained in severely psychoneurotic persons. It goes without saying that intense and competent psychotherapy should be a prerequisite for all neurotic patients prior to lobotomy, in the same way as adequate shock therapy is for schizophrenic patients. Neurotic persons

who have not benefited from psychotherapy should be accepted for the operation if they are total invalids, suffer severely and are unable to lead a normal life.

Patients with personality disorders, such as psychopathic personality, are often presented to us for lobotomy. The fact should not be overlooked, however, that the operation can never change personality traits. Dangerous tendencies justify the operation occasionally in such conditions as mental deficiency, psychomotor epilepsy, and other organic conditions, but more individual case reports including failures should be published in detail in order to assist psychiatrists in the selection of such cases.

Long range therapeutic planning is of primary importance since more therapeutic procedures are available. It is our definite impression that integration of lobotomy with the other methods at our disposal will definitely increase the number of successfully treated patients in psychiatry.

DISCUSSION

DR. JOSEPH A. WINN: I should like to ask whether Dr. Kalinowsky and Dr. Scarff have had experience with lobotomy in neurologic disturbances with intractable pain.

DR. JAMES LAWRENCE POOL: Have you any patients who have recovered completely from delusions and hallucinations?

DR. LOTHAR B. KALINOWSKY: We have had no experience with intractable pain that I can discuss.

Dr. Pool's question is very interesting, and it raises a point that puzzles me more than anything else. There are patients who recover from delusions and hallucinations. Many of these have chronic conditions, and it is an old experience in psychiatry that delusions and hallucinations often disappear in persons with chronic schizophrenia when they deteriorate. Since so far the schizophrenic patients who have been submitted to us for operation have mostly had chronic conditions of five, ten or more years' duration, their hallucinations and delusions were not very definite and disappeared after operation. I think that up to a certain point delusions and hallucinations are kept up by the emotional responsiveness of the patient, but when the operation removes most of their affectivity the delusions and hallucinations disappear entirely. A more interesting fact is that after lobotomy, unlike shock therapy, even in cases with otherwise good result, the delusions and hallucinations often do not disappear, and this invites some speculation. I feel that in shock treatment one attacks the disease process, wherever it may be localized, whereas in lobotomy one obviously does not. It is interesting that in one of our best cases severe hallucinations and delusions disappeared completely for one year; there were hardly any side effects present, and the patient even went back to college. After one year the patient had a relapse of all symptoms, severer than we had seen in any other case. I do not know how to explain this.